Bk. 4

W. RALL

4

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Mostly 1964 Research Diary 6/19/63

The purpose of this record is to collect notes & outlines presently on loose sheets of paper, with a view to a more efficient dispatch of unfinished papers based on accumulated computations. Basic problem seems due to two principal factors:

(1) evolving research interests

(2) priority given to invited papers.

Solution would seem to lie in brief papers instead of buried notes.

(This comment follows not long after completing Ojai manuscript)

Here is copy of list prepared 2/13/62 just before Wash. Biophys. Soc. Meeting

① Complete basic potential distribution paper
  ⓐ This involves completion of figures
  ⓑ new introduction

② Membrane potential to be dealt with in a separate paper. This could include: Sum of series approach and a brief recap of σ_e and σ_i of 1953 abstract (relation of σ_e & σ_i to Re and Ri). Also integral for case of linear fcn of r for extracellular source weights. Also discuss isopotentiality of soma membrane.

③ Paper with Ezra & Jeanne

④ Spherical Symmetry case as in Stockholm: expanded

⑤ Computations for pyramidal cells

⑥ Computations for generator potential with $\rho \neq \infty$

⑦ Also for finite dendritic length.

⑧ Computations for synaptic E & J for $\rho \neq \infty$

⑨ Current step to soma for finite dendritic length & $\rho \neq \infty$

⑩ Paper with Aitken, or at least theory

⑪ Dendritic E & J transfer functions (? approx)

⑫ ? Fuortes model. — Nelson, Terzuolo — Voltage Clamp Model

3/11/64

Now to continue as Research Diary

This will be Bk. 4 to continue from Bk 3, just filled.

Bk. 1 is so far incomplete record of 1959–1962 computations
Being reconstructed from loose notes of work with
Ezra, Jeanne, Witmer, Brunelle & early H-800

Bk. 2 record of Compartmental Computations with
Berman-Weiss program 7/62 – 63
Includes calcs for Ojai & also degeneracies &
early exploration of non-linear systems.

Bk. 3 record focussed on Propagation Computations
11/63 — 3/64 but gradually transformed into
a running research diary with numbered pages.

3/11/64

The list of unfinished papers has grown during the past two years (i.e. since the list of p.1 was prepared)

Item ⑧ and part of item ⑪ were taken care of in the Ojai manuscript prepared a year ago & recently read in page proof.

With Gordon Shepherd, the Aitken material is being pushed into publishable form. Also, new theoretical result on pp 83–88 of Bk 3, on averaging equally probable depths.

However have much new material to be worked up for publication: (see pp 89 of Bk 3, or p.5 below)

esp. Theory for Ve in cortical layer
Application to Olfactory Bulb
Model for propagation, & its analysis
(see pp 91 & 93 of Bk 3)

Also miniature epsps
Impedance effects of remote synaptic activity.
(partly in relation to Tom Smith)
Extracell pots. of motoneuron populations
(as brought up again by Van Buren) p. 92 in Bk. 3

Also in progress is tree generation with Farlow & Graber

Bk 3 pp 65, 75,

Note that Aitken's letter of 1st March 1960 estimated order of 20% shrinkage, overall for the large blocks used.

$$(0.80)^{3/2} = 0.715$$

$$\boxed{(1.25)^{3/2} = 1.4}$$

true dendritic conductance would be 1.4 times that calculated without a correction for shrinkage.

3/12/64 Re Extrap. of Dendritic Branching

Note that former WXR603C with WXR67C was recently revised & recompiled as WXR604C with WXR68C. Compiled without trouble, but system could not load (system error). Finally overcome 3/9/64 – 3/10/64.

This new version provides for TRFAC = factor correcting for trunks not seen.

Also, computes ratio of extrap. surface area to seen surface area.

Also, prints out the rescaled electrotonic lengths each time

Also computes { RNBAX, RNTWAX, RNINF
& prints { GNBAX, GNTWAX, GNINF

Wrote Aitken on 3/5/64 to inquire specifically about perikaryon depths; whether cutting perikarya can or cannot be ruled out, and about section thickness for kitten cells.

Using $\bar{f} = \dfrac{\sqrt{h^2+2h|x|+b^2} - b}{h+2|x|}$ from p. 87 of Bk. 3

Consider two cases for kitten cells

$h=100$, with $b=25$, $|x|=10$

$$\bar{f} = \frac{\sqrt{126.25} - 2.5}{10+2}$$
$$= (11.25 - 2.5)/12$$
$$= 8.75/12 = 0.729$$
$$= 1/(1.38)$$

for $|x|=0$

$\sqrt{106.25}$ etc

$$\rightarrow (10.3 - 2.5)/10 = 0.78$$
$$= 1/(1.28)$$

$h=200$, with $b=25$, $|x|=10$

$$\frac{\sqrt{446.25} - 2.5}{20+2}$$
$$= (21.12 - 2.5)/22$$
$$= 18.62/22 = 0.846$$
$$= 1/(1.18)$$

for $|x|=0$

$\sqrt{406.25}$ etc

$$\rightarrow (20.15 - 2.5)/20$$
$$= 0.8825 = 1/(1.135)$$

People to write or talk to:

- Tom Smith
- FitzHugh
- Aitken
- Braitenberg
- Kathryn Thomas (Minnesota)
- Dun Fu Tang

3/12/64

Papers to be completed (list from p. 89 of Bk 3 dated 3/4/64)

6 page note for Eccles Commemorative Volume 8/11/64
Dendritic Synaptic Patterns: Experiments with a Mathematical Model

Paper on Branching Extrapolation for Dendritic Radial Symmetry
" " Dendritic Surface Area Estimates from Aitken's Data
" " Dendritic Input Conductance " " " "
" " Analysis of Sholl's data

Theoretical Dists of Ve & Vi for spherical soma
" " " Vm " " "
" " of Ve for asymmetric dendrites (Ezra & Jeanne)
" transients for radially sym (Stockholm 10 min paper)

& relation of Vi, $\partial V_i/\partial x$, Im, Ve, etc.

Theory for Ve with synch. act. in cortical layer

Comparison of Theory & Expt. for antidrom. in Olfac. Blb

Math. Model for Comput. of Action Potential Propagation
into Regions of Changing Geometry & Safety Factor
(maybe break in Two?)

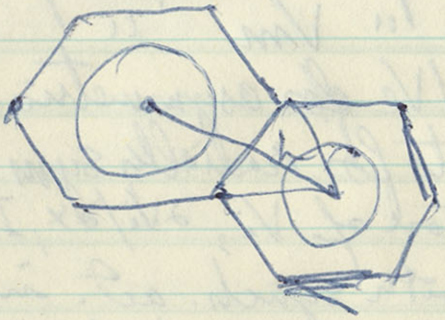
Calc of miniature epsp generated at different locations (cf Katz)
& locations & degeneracies & effect of β value.

? Hypothesis on synaptic plaques

? Hypothesis on core conductance changes

Diagrammatic & descriptive of single cell, populations,
layers, synch. activity.

As of today. Need to prepare annual report.



$h = L/2$

area of equilat. Δ is $\frac{1}{2} b h$

where $h = \sqrt{b^2 - \frac{1}{4} b^2} = \frac{\sqrt{3}}{2} b$

or $\frac{1}{2} b = \frac{1}{\sqrt{3}} h$

$\therefore$ area of $\Delta = \frac{h^2}{\sqrt{3}}$

and area of hexagon $= \frac{6h^2}{\sqrt{3}} = \frac{6L^2}{4\sqrt{3}}$

3/18/64

Calculation to relate synaptic contact area as proportion of total area, to contact ratio in profile. Need to assume some sort of model. Suppose at first the contact areas are circular and their centers are arranged according to a hexagonal lattice over the dendritic surface. If d is the diameter of each circle and L is the distance between centers, one would expect the average profile ratio of contact to total to be d/L, while the ratio of contact area to total area would be

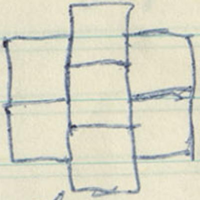
$$\frac{\text{area of circle}}{\text{area of hexagon}} = \frac{\pi d^2/4}{6L^2/(4\sqrt{3})} = \frac{\pi\sqrt{3}}{6}\left(\frac{d}{L}\right)^2$$

$$= 0.907\left(\frac{d}{L}\right)^2$$

$\therefore$ if $\frac{d}{L} = 1$, get 0.907 for inscribed circle in hexagon

If contact area is also hexagonal, get $(1)\left(\frac{d}{L}\right)^2$

In general, for other lattice, such as



if contact area is assumed to have same shape as the lattice element, get $\left(\frac{d}{L}\right)^2$

if shape is different, get some factor less than unity $* \left(\frac{d}{L}\right)^2$

All this relevant to Kathryn Thomas's % membrane area covered by synaptic endings.

3/18/64

A day or two ago, got phone call from Mr. Koenig who has a large analog computer in Engineering firm behind the GEM store 949-3900

Computer belongs to Govt. They teach a course in systems engineering with it. Manufactured by Applied Dynamics, Inc. - 152 op. amplifiers, also function generators & multipliers.

Might be useful to me to explore ranges of parameters which keep system in same domain.

Yesterday, prepared rough draft of annual report.

Also prepared description of branch generation problem for Betty Gorbr. She reports that program is presumed to be OK. But there is still an unresolved difficulty in getting plotter input.

On Third Thought (3/27/64), it may lead to too many complications to try to take care of anodal break & everything else. It may be better to keep model very simple for propagation calculations. This may not be the time to complicate this model.

Intuitively, it seems to me that anodal break would require changes such that $J \neq 0$ for resting conditions, hence, also, $E \neq 0$. hence, also, might change normalization of V, but all this would lose much of the simplification.

Try, with present program, reducing RINB by factor of 10
and QENCHB by factor of 10

to see if can raise threshold & also falling phase of spike.

3/26/64 Yesterday had lunch with Rashevsky & Zinn. Conversation stimulated me to test my impulse model further

for single path
$$\tau \mathring{V} = -(1+\varepsilon+g)V + \varepsilon + \beta g + \psi$$
$$= \varepsilon(1-V) - g(V+\beta) - V + \psi$$

$R_1 V^3$
$$\tau \mathring{\varepsilon} = (RA)V^2 + (RB)V^4 - [(RC) + (RD)g]\varepsilon$$
$$\tau \mathring{g} = (RE)[(RC) + (RD)g]\varepsilon - (RF)g$$

from p. 93 of Book 3, estimate ~~RC ≈ 20~~

R_1 = RACT * RINB ≈ 3×10^4
RC = ROUTB ≈ 20
RD = QENCHB/QENCHA ≈ 3
RE = QENCHA/RACT ≈ .033
RF = ROUTC ≈ 3

peak $\varepsilon \approx 450$
peak $g \approx 50$

for $V = 0.1$, $k_1 V^3 = 3 \times 10^4 \times 10^{-3} = 30$
approx threshold.

Want higher thresh so that $(RA)V^2 + (RB)V^4 \approx 30$
for $V \approx 0.25$

✓ $RB = 3 \times 10^4$

$RB(.25)^4 \approx (3 \times 10^4)(4 \times 10^{-2}) = 1200$
$(.0625)^2$
$(.039)$

$RB(.2)^2 \approx (3 \times 10^4)(16 \times 10^{-4}) = 48$

Could start out by trying 3×10^4

WXR605C first explored the area correction, but did this for XAJL as well as XAJH.

Then, when revised to WXR606C, removed the area correction XAJL → XASJL

and added the TH for TB change in conductance calculation

Can now delete WXR605C
& later 604C & 68C

3/27/64

Things to do soon

Add giant extracellular to WXR791C (p.80 of Bk 3)

? Question of threshold level in current calcs with (791C) may want to use $k_1 V^2 + k_2 V^4$ instead of $k V^3$ (p. 79 Bk 3)

Note that on p. 79, two cases almost suitable, but want A & B also, subst for .0669 better, I.C. like .0659

Note point about anesthesia & facilitation for antidromic invasion on p. 77 of Bk 3,

Should duplicate WXR791C, 91C, 92C, 82C because works well & now want to revise

? Also Tom Smith

Also, any new figures for Eccles Volume
? Write Archie

Also, note: Recently successfully modified to get WXR606C WXR69C

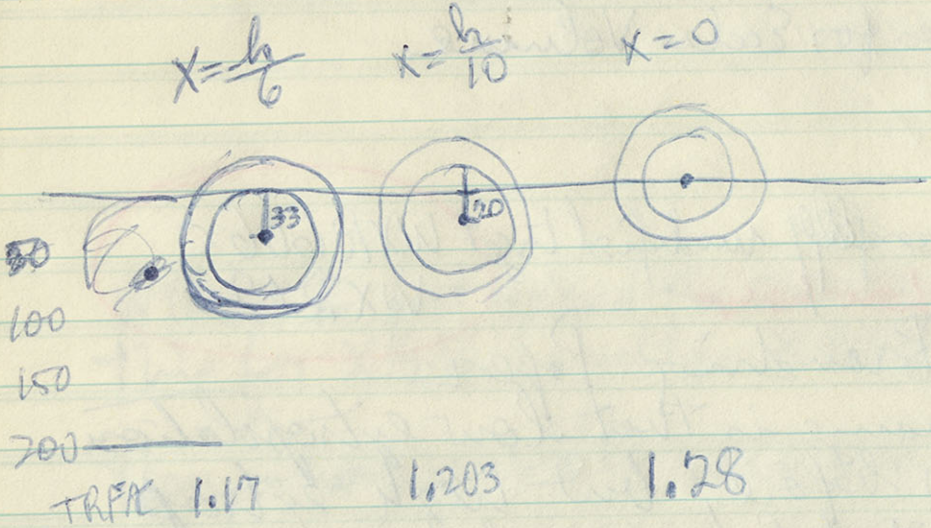
Highhigh vs Low Low

for Dendritic Branching Paper

The essential change is that low extrapolation is as it was before, but high extrap now uses total seen for areas and for lengths, whenever this is larger than extrap from bifurcating (also ambig treated as cut)

Thus, for BINB, use TH = tanh (Z(J,5)) when Z(J,5) > Z(J,2)

And for areas, use XAJH = XASJH = ASJ * FACJH previous when this exceeds XAJH = FACJH current * π * SDXL(J,2)


x = h/6
x = h/10
x = 0
33
20
80
100
150
200
TRFAC
1.17
1,203
1.28

3/30/64

Letter from Aitken says that ~~he~~ is prepared to regard perikaryon depth as unknown but within the limits 200μ. "Cut cells would appear as fragments and were *not* counted."

I can see how the small piece is a fragment, but how about the large piece.

∴ using formula on page 84 of Bk 3

Conservative case $X = \frac{h}{12}$ gives $\bar{f} = 0.854$, TRFAC = 1.17

If $X = \frac{h}{10}$, corresp to 20μ, i.e. 15μ of 35μ radius cut off.

Volume of spherical segment $= \frac{1}{3}\pi \cancel{Z}h^2(3r - \cancel{Z}h)$

Volume of sphere $= \frac{4}{3}\pi r^3$

$$\frac{h^2(3r-\cancel{Z})}{4r^3}$$

$\cancel{Z}h = 15\mu \rightarrow 3$, $r = 35\mu \rightarrow 7$

$X = 20$

$$\frac{9(21-3)}{4\cdot 7^3} = \frac{9\times\overset{9}{\cancel{18}}}{\underset{14}{\cancel{28}}\cdot 49}$$

$$= \frac{81}{686} = .118$$

approx 12% vol.

$h = 20$, $x = 2$, $b = 5$

$$\bar{f} = \frac{\sqrt{(18)^2+5^2} - \sqrt{4+25}}{20-4}$$

$$= \frac{\sqrt{324+25} - \sqrt{29}}{16}$$

$$= \frac{18.69 - 5.38}{16}$$

$$= \frac{13.31}{16} = 0.83_2 = \frac{1}{1.203}$$

probability of cut perikaryon is ~~100~~ $\boxed{\frac{13\mu}{80\mu}}$ 16%

uncut perikaryon $\boxed{\frac{67}{80}} = 84\%$

#1, 16, 22, 57, 58

quite likely these are the ones whose → truncation happened to leave no reference tree long enough to permit further extrapolation. In that case, the longer ones may be closer to the truth.

4/3/64

Found yesterday, in examining Aitken's 10 neurons, that dendritic surface area percentages with order of branching are probably better expressed separately for two groups of five.

	Trunks	Prim	Sec	Tert	Quat	Quin	Sex
Longer Cells	9%	16	21	19	20	13	2
Shorter or More cut off	18	31	34	17	0	0	0

Also discussed with Gordon at length about my old ditto where weighted mean of L/λ is estimated from

$$\frac{L}{\sqrt{d}} = \frac{\Sigma Ld}{\Sigma d^{3/2}}$$

where $d^{3/2}$ is the weight.

Wrote memo to Betty Garber about calc. of mean lengths.

Plan to write letter to Kathryn Thomas about above percentages.

Also, may wish to modify WXR 606C to provide $\frac{SD}{N}$ and $\frac{SL}{N}$ for all categories.

May need $\frac{SL}{N}$ & St. dev of length for comparison with the generated trees.

4/7/64 Conversation with José began with relation between Laplace transform + Fourier transform.

Laplace transform mapping from half plane $R(s) \geq 0$

Then the factor e^{-st} can tame mild blow up of a fcn

$$f(s) = L\{F(t)\} = \int_0^\infty e^{-st} F(t)dt$$

suppose $F(t) = e^{at}$ which blows up ~~at~~ $t \to \infty$
and its transform, $\frac{1}{s-a}$ has a pole at $s = a$

Therefore simple integration possible only for $s > a$, and integration around the pole gives e^{at}

His point, was that if there is no pole for $s > 0$, then can integrate along imaginary axis; ~~[illegible]~~ then this is exactly equal to the Fourier transform.

Then we got to talking about whether one can get from a Bode diagram (which applies to A.C. steady state) back to complete transform which gives transient solutions. In principle, yes, because analytic fcns in complex plane are such that all can be recovered from a precise defn in a small portion of complex plane. But what about in practice. Our thought was, suppose we set up a model which fits Bode, except we miss a pole far out in rt. half of ~~complex~~ plane. What will this error due to the computed transient response?

$$\text{Rapprox} - R = R' - (q+1) R$$

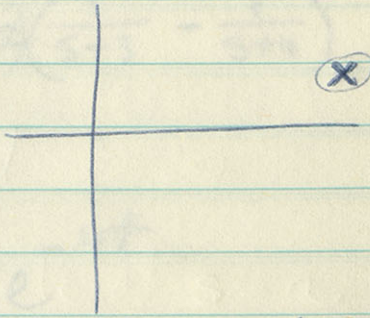
4/7/64

This led to the following conjecture about cancelling a pole in complex plane:

Consider $F \longrightarrow \boxed{W} \longrightarrow R$

forcing fcn weighting fcn response

Suppose $\mathcal{L}\{W\} = \dfrac{1}{(s+a)(s+b)(s-\underset{\text{pole}}{\lambda})}$



Then pole will be cancelled for response, provided that $\mathcal{L}\{F\}$ has $s-\lambda$ in the numerator

say $\mathcal{L}\{F\} = \dfrac{s-\lambda}{(s+c)(s+d)}$

Then $\mathcal{L}\{R\} = \dfrac{1}{(s+a)(s+b)(s+c)(s+d)}$

which has no pole

This means that although $W(t)$ blows up
$R(t)$ does not
provided $F(t)$ fits above

Also, now, if $\mathcal{L}\{W_{approx}\} = \dfrac{1}{(s+a)(s+b)}$

then $\mathcal{L}\{R_{approx}\} = \mathcal{L}\{F\} \cdot \mathcal{L}\{W_{approx}\}$

$= (s-\lambda) \cdot \mathcal{L}\{R\}$

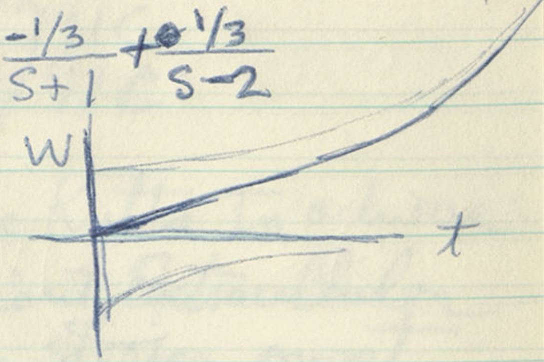
$R_{approx} = R' - \lambda R$

RKopp

4/7/64

e.g. suppose $L\{W\} = \frac{1}{(s+1)(s-2)} = \frac{-1/3}{s+1} + \frac{1/3}{s-2}$

then $W = \frac{1}{3}(e^{2t} - e^{-t})$

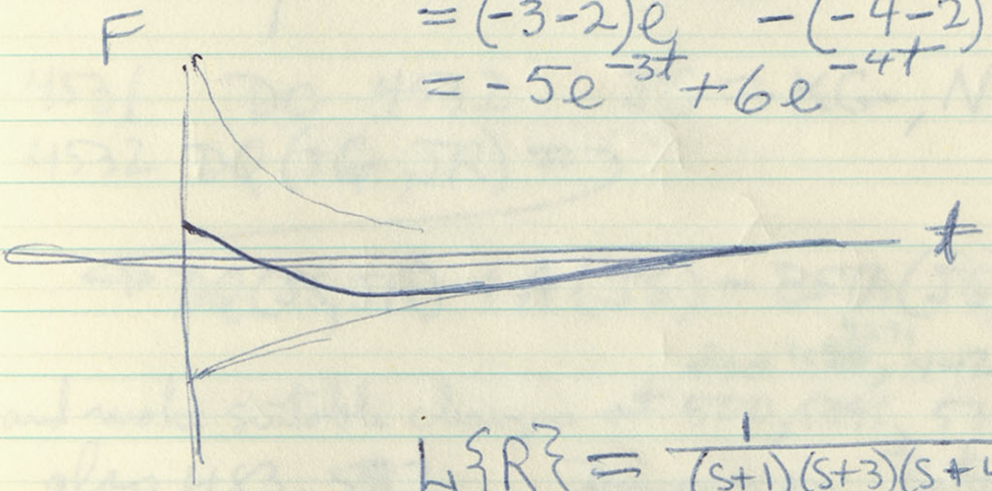


Suppose $L\{F\} = \frac{s-2}{(s+3)(s+4)} = (s-2)\left(\frac{1}{s+3} - \frac{1}{s+4}\right)$

$$F = (D-2)(e^{-3t} - e^{-4t})$$

$$= (-3-2)e^{-3t} - (-4-2)e^{-4t}$$

$$= -5e^{-3t} + 6e^{-4t}$$

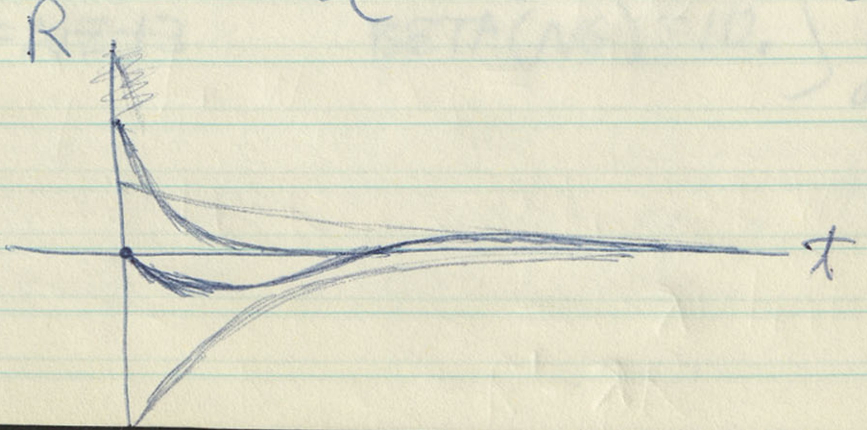


$$L\{R\} = \frac{1}{(s+1)(s+3)(s+4)}$$

$$= \frac{+1/6}{s+1} - \frac{1/2}{s+3} + \frac{1/3}{s+4}$$

$$R = \frac{1}{6}e^{-t} - \frac{1}{2}e^{-3t} + \frac{1}{3}e^{-4t}$$

$$= \frac{1}{6}(e^{-t} - 3e^{-3t} + 2e^{-4t})$$



4/15/64 WXR793C mod of 791C
WXR 93C mod of 91C

Modified Main program & one Runge Kutta to achieve two purposes I Include Giant Extracellular
II Use V^4 for steeper onset

$$\frac{d}{dt}(V_g - V_e) = \frac{d}{dt}(V_i - V_e) + (V_i - V_e) - \beta(V_g - V_e)$$

Thus we put in WXR93C

```
4531  DO 4532   JG = KG, NG
4532 DQ(JG, JR) =
        DQ(JS, JR) + A(JS) - BETA(JG) * A(JG)
```

and make suitable changes at 500, 5091, 530, 5391, 560, 5691 also $\overset{4291}{420}$, 442
also 483, 582. Dimension ^{2}Beta (14)
Equivalence (R1NB, RBSQ), (R1NC, RBFR)
might cause trouble

Define KG = NZ + 1 BETA(KG) = 2.
LG = NZ + 2 BETA(LG) = 5.
NG = NZ + 3 BETA(NG) = 10.

in main program and add to argument

4/16/64 WXR793C

First test did not work well: compiled OK
made further corrections
also added G fudnot V^4 to 92C → WXR94C

New test also did not work well, V(JZ=2)
does not seem to get anywhere.

4/20/64 putting in new tests with
NT = 11 and IFTEST = 81 or 11
for detailed checkout

Prepared abstract for J. Johnson

Wrote letter to Kathryn Thomas
(Minnesota)
summarizing area results.

Read but did not write comments on
Lamria's coupling coefficients.

Discussed + proof read manuscripts
with Gordon Shepherd. Attempt
to complete next week.

4/21/64 **WXR793C** still not working well.

Most obvious difficulty is that DQ(JZ, JR) does not depart from zero for JZ from 2 thru JH

This test was in 94C, apparently 472 & 473 were not carried out.

Retest both in 791C & 793C
putting initial values in all compartments.
At least this will also provide test of GVe.
Also, will learn more about failure of 472 & 473

Eureka! I just found the trouble, argument of 94C & 93C was UA, UD, USA, USD from duplication of Call argument, whereas the subroutine uses GA, GD, GSA & GSD.

Must either change argument or use equivalence statement.
Simplest to use equivalence
but might as well await the results of this test, to see if GVe works & also if V^4 works.

4/27/64 WXR793C

GVe worked for passive case, where still used cube function, but active case WXR93C went negative. Decided to eliminate Equivalence statement for RBSQ and RBFR and take care of this with arg.

GVE for Beta = 2. seemed to have too flat an after neg. Also, the scale changes for JG = LG & NG were too restricted.

∴ Change Beta (KG) = 5.
LG = 10.
NG = 20.

and keep all GVe plotting scales -.4 to +.7

test put in today for IFVE = 1 for passive case.
also test active case with repaired arg.

4/23/64 – 4/27/64 WXR611C

Modified WXR606C to compute the average & std. dev. of lengths, drams & prod of lengths & drams for J, K

~~Also overall~~ Both for each cell & for groups of cells divided by two finis cards. Needs 3 finis cards at end.

NJCELL(JCELL) stores cell nos. of a group.

Added many dimensions.

Used formula $Var(x) = \frac{\Sigma x^2 - m \Sigma x}{N(N-1)}$

Thus VARD = (SDSQ(J,K) – AVD(J,K) * SD(J,K)) / Y

where Y = N(N-1)

Worked out 4/23 & 4/24

Made corrections 4/27

4/30/64

Problem 64793.0011

for K.V.E = 2 compare soma extracellar Col 4
with guard (Beta = 400) Col 11

$V_g - V_{midiff.}$
at KT = 19, guard corresp to 2 mV
soma Ve corresp to −1 mV

which agrees with $V_g - V_e = 3$ mV at this time

This implies that $\beta = 400$ is far from negligible

i.e. referring back to page 80 of Book 3

$$\beta = \frac{R_g + R_m}{R_g} \quad \text{where} \quad R_g = AR_d$$

that $\frac{R_m}{R_g} \simeq 400$ is far from negligible

In other words, a negligible R_g is $\ll R_m \times 10^{-3}$

However, convergence resistance may be sufficient to account for a negligible R_g & for a non-negl. R_g if R_m is reduced.

G Ve shapes look very promising.

$$\frac{dV_i}{dt} + \frac{V_i}{R_m^* C_m} = \frac{dV_g}{dt} + \frac{V_g}{R_g C_m}$$ for $R_m^* \gg R_g$

$$\boxed{\frac{dV_i}{dT} + \gamma V_i = \frac{dV_g}{dT} + \beta V_g}$$

where $\gamma = \frac{R_m}{R_m^*}$

$\beta = \frac{R_m}{R_g}\left(\frac{R_m^* + R_g}{R_m^*}\right)$

4/30/64 – 5/1/64 Giant Extracellular

for Rm normal, the D.E. is (for Ve as reference)

$$\tau \frac{dV_i}{dt} + V_i = \tau \frac{dV_g}{dt} + \underbrace{\left(\frac{R_m + R_g}{R_g}\right)}_{\beta} V_g$$

If $R_m \gg R_g$, then can use $\beta \approx \frac{R_m}{R_g}$

Suppose normal condition is something like $\beta = 10^4$

Suppose Rm falls by factor of $100 = \gamma$
then τ falls by factor of 100

by $T = t/\tau$ for normal τ

Then $$\tau^* \frac{dV_i}{dt} + V_i = \tau^* \frac{dV_g}{dt} + \left(\frac{R_m^* + R_g}{R_g}\right) V_g$$

multiply through by γ to get

$$\frac{dV_i}{dT} + \gamma V_i = \frac{dV_g}{dT} + \gamma \left(\frac{R_m^* + R_g}{R_g}\right) V_g$$

To be exact, get $$\frac{dV_i}{dT} + \frac{R_m}{R_m^*} V_i = \frac{dV_g}{dT} + \frac{R_m}{R_m^*}\left(\frac{R_m^* + R_g}{R_g}\right) V_g$$

But good enough approx is

$$\boxed{\frac{dV_i}{dT} + \frac{R_m}{R_m^*} V_i = \frac{dV_g}{dT} + \frac{R_m}{R_g} V_g}$$

for Giant, suppose $\qquad 10^2 \qquad\qquad 10^4$

5/1/64 Plan to modify program to

Compute $\frac{dV_g}{dT} = \frac{dV_i}{dT} + \gamma V_i - \beta V_g$

where $\gamma = \frac{R_m}{R_m^*}$ R_m is normal, R_m^* is abnormally reduced

and $\beta = \frac{R_m}{R_g}\left(\frac{R_m^* + R_g}{R_m^*}\right) \approx \frac{R_m}{R_g}$ for $R_m^* >> R_g$

where β is normally of order 10^3 to 10^4

try $\beta = 10^4$ with $\gamma = 1, 10, 100, 1000$

4/28/64

23

5/1/64 Summarize 64793

64793.0001 — .0005~~7~~6 developed program

64793.0006 proved that NSTEP=2 was too small for hot kinetics

64793.0007 first good GVe for passive case
also extracellulars $\beta = 2., 5., 10.$

64793.0008 good slightly delayed soma spike - passive case
β values 320, 160, 80, 40, 20, 10

64793.0009 first successful active case NSTEP=4
GVe for $\beta =$ 100, 30, 10

RBFR=120 Here, because of hot kinetics $\beta = 30$ gave $\simeq$ 80mV peak to peak
$\beta = 10$ gave >100mV
$\beta = 100$ gave nearly 40

64793.0010A RBFR=80 soma blocked at 20mV
because of no residual facil.

64793.0010B put residual facil in soma & dendrites
avoided block, quite good shape
good GVe for $\beta = 25, 50, 100, 200, 400$

64793.0011 passive case with residual facil.
β values of 100, 200, 300, 400

Also extracellulars

5/1/64

WXR611C worked fairly well on 4/30/64

Got correct averages & st. deviations

However, group totals loused up when one of group has JMP < JMPOP

Can solve this either by using only groups with all JMP the same, or better still,

~~at 830 DO 835 J=1, JMP~~

replace 830 with implicit do from J=1 to JOMP

Then set J = ~~JMP~~ 10 and I = ~~10~~ JMP
and change J to I in last term of each of these expressions.

~~Then 145 et seq have to be DO J=1, 30~~

change JMPOP to JOMPOP

and at 885 use J=1 to JOMPOP

and then use J=10

X=JCELL
FN=1./X

Do area extrap with SD(J,K) = ~~AVN(J,K)*AVD(J,K)~~ PSD(J,K)*FN

SDXL(J,K) = ~~AVN(J,K)*AVDXL(J,K)~~ PSDXL(J,K)*FN

5/6/64

on 5/5/64 overran limit of number of fixed consts & non-dimensioned variables

Took care of this, but on 5/6/64 still had to make a few small corrections

at 21 made J=1, 10 instead of 1, JMP
because bin 10 was in trouble

at 542, 543, 544 restored PRED, PREXL

at 3221 set JOMP = JOMPOP
3222 X = JCELL
323 FN = 1./X
because apparently FN = 1/JCELL = 0

Now hope for success.

Also had to change J to L in statement 837

Finally got good result 5/8/64

5/6/64 WXR793 compiled & worked with Beta & Gamma ~~9~~ RBSQ, RBFR in 94C

However, got blow up for some G Ve; suspect due to I.C. in soma.

New runs will avoid this.

Got interesting result comparing different combinations of β & γ

$\frac{\pi}{2} = 1.5708$ $\frac{2}{\pi} = 0.6366$ 2 Dimen

$\frac{4}{\pi} = 1.2732$ $\frac{\pi}{4} = 0.7854$ 3 Dimen

5/8/64

Problem of Ratio : $\frac{\text{projected length}}{\text{true length}}$ of randomly oriented branches.

For branches lying in laminar planes, then answer is $\frac{2}{\pi}$

For branches dist. in three dimensions, answer is $\frac{\pi}{4}$

Betty Garber's first calc of tree, 6 trunks, 6 orders giving total of 378 elements

$\frac{\text{true}}{\text{Y-Z proj}} = 1.2547$

$\frac{\text{True}}{\text{X-Z proj}} = 1.3049$

$\frac{\text{True}}{\text{X-Y proj}} = 1.2399$

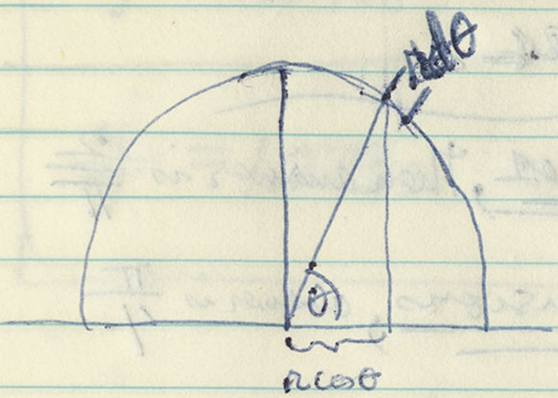
$3 \,\big|\, 3.7995$

1.2665

which agrees rather well with $\frac{4}{\pi} = 1.273$

It was this numerical result which led me to clarify the difference between the 2-D and the 3-D assumptions. Long ago, both Ramon-Moliner and I had thought the $\pi/2$ answer was correct, because of the specious argument that a plane is a fair sample of 3-D.

2-D



Suppose N radii are distributed uniformly ~~with respect to~~ around the quarter circle

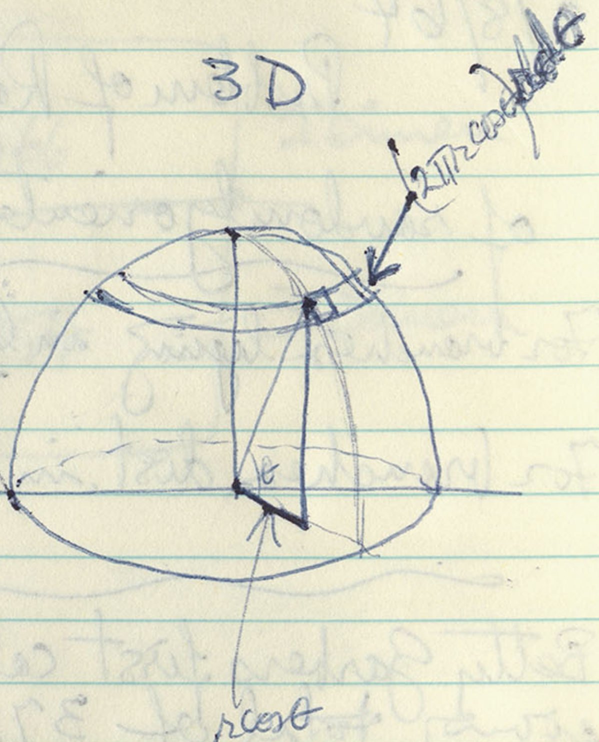
Then the number expected ~~from~~ between θ and θ+dθ can be expressed

$$N\frac{d\theta}{\pi/2}$$

any arbitrarily chosen branch has a probability $d\theta/\frac{\pi}{2}$ of laying in this interval

The probability density (per radian) that any arbitrarily chosen branch will lie at any particular point is $\frac{2}{\pi}$
value of θ

3D



Suppose N points are dist. uniformly over the surface of the hemisphere

Then the number expected to lie in the surface annulus from θ to θ+dθ can be expressed

$$N\frac{2\pi r^2\cos\theta d\theta}{2\pi r^2}$$

any arbitrarily chosen branch has a probability $\cos\theta\, d\theta$ of laying in this annulus

The probability density (per radian) that any ~~arbitrary~~ point will lie at θ is $\cos\theta$

5/8/64

For any given instance, $l = r\cos\theta$, $\frac{l}{r} = \cos\theta$

To get the mean value of $\frac{l}{r}$, we must evaluate the integral

$$\text{mean}\,\frac{l}{r} = \int_0^{\pi/2} \cos\theta \cdot p(\theta) \cdot d\theta$$

where $p(\theta)$ is the probability density (per radian)

For the 2-D case, $p(\theta)_{2D} = \frac{2}{\pi}$

$$\text{and mean}\,\frac{l}{r} = \int_0^{\pi/2} \frac{2}{\pi}\cos\theta\, d\theta = \frac{2}{\pi}\Big[\sin\theta\Big]_0^{\pi/2} = \frac{2}{\pi}$$

For the 3-D case, $p(\theta)_{3D} = \cos\theta$

$$\text{and mean}\,\frac{l}{r} = \int_0^{\pi/2} \cos^2\theta\, d\theta = \left[\frac{\theta}{2} + \frac{\sin 2\theta}{4}\right]_0^{\pi/2}$$

$$= \frac{\pi}{4}$$

* * *

Apparent paradox: suppose we choose θ and ψ independently from uniform distributions, then $p(\theta)$ and $p(\psi)$ are both constants. But, then the resulting points are not uniform over the sphere; they are concentrated near the poles.

Try

$$\begin{array}{cccccc} & \beta=100 & & \beta=100 & & \beta=50 \quad 25. \\ & & \longleftarrow & & \longrightarrow & \\ 4 & \gamma=2 & & \gamma=1 & & \gamma=1 \end{array}$$

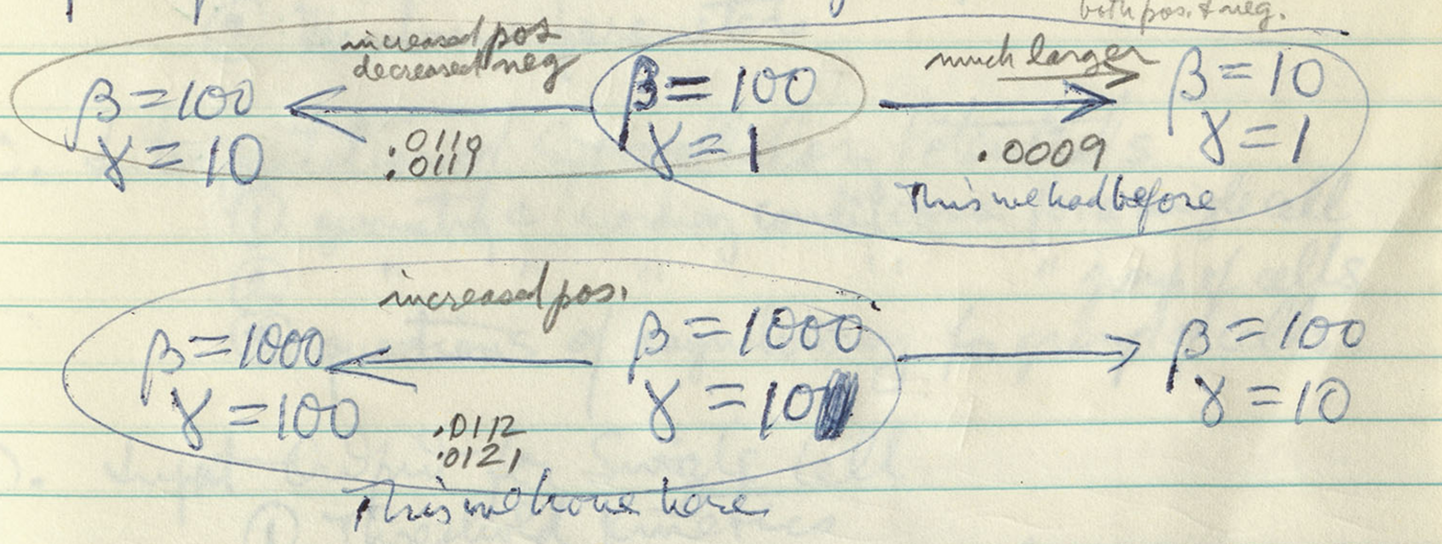
5/8/64

64793.0112 & .0121

Did not avoid blowup with zero initial conditions in soma. Apparently need to decrease Runge Kutta Step Size to handle such large values of β.

The intention was to begin with large β and compare the effects of { ⓐ decreasing β / ⓑ increasing γ

Can use smaller step size. However may be useful to rephrase problem so that we compare perhaps with results we already have



Maybe should use factors smaller than 10. Perhaps 2 or 4, once well centered.

5/11/64 Perspectives on Kinds of Problems: Math. Models & Neurophysiol

A. General Model of Neuron with different simplifications for different purposes.
  ① Geometric simplifications
    ⓐ axon
    ⓑ equivalent cylinder to class of dendritic trees
    ⓒ specific types of dendritic trees.
  ② Simplifications of Membrane Kinetics.
    ⓐ passive membrane
    ⓒ step changes in parameters
    ⓓ time varying resistances $\propto$ on V & t.

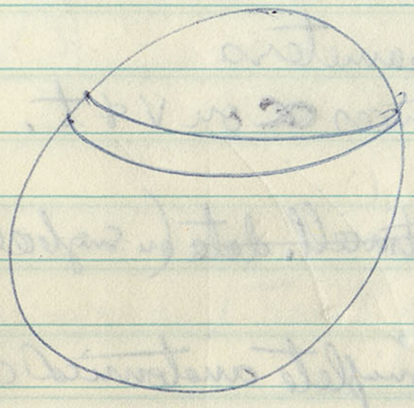
B. Estimation of model parameters from intracell. data (on single cells).
  ① Geometric parameters
    ⓐ interpretation of incomplete anatomical data
  ② Membrane parameters

C. Interpretation of Extracellular Potentials
  ① geometry & recording conditions for a single cell
  ② " " " " " group of cells
  ③ questions of asynchrony for group of cells.

D. Input-Output for Single Cell
  ① Threshold Kinetics
  ② Patterns of synaptic activity

E. Interactions ~~of~~ within a Group~~s~~ of Cells

F. Interactions between different groups of cells



$$dA = (2\pi R \cos\varphi)\, R\, d\varphi$$

$$= 2\pi R^2 \cos\varphi\, d\varphi$$

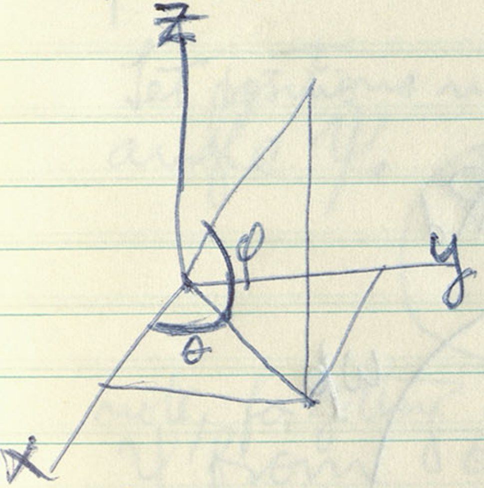
$$= 2\pi R^2\, d(\sin\varphi)$$

uniform A means uniform $\sin\varphi$

5/18/64 Gave talks to computer group on 5/13/64

Also worked on problem of having orientations equally probable wherever they are supposed to be. Roughed this out 5/14/64 and presented notes to Betty Garber on 5/15/64. However, there was an error. Here now correct..

For Trunks



φ is lattitude

θ is longitude

$x = R \cos\varphi \cos\theta$

$y = R \cos\varphi \sin\theta$

$z = R \sin\varphi$

These are ~~they~~ the symbols used in program.

Before 5/15/64, the original program chose

φ from a uniform dist from 0 to 2π

θ " " " " " 0 to π

Also, one of daughter direction cosines was chosen from a uniform distribution.

Revised program let RAND be random number from 0 to 1.

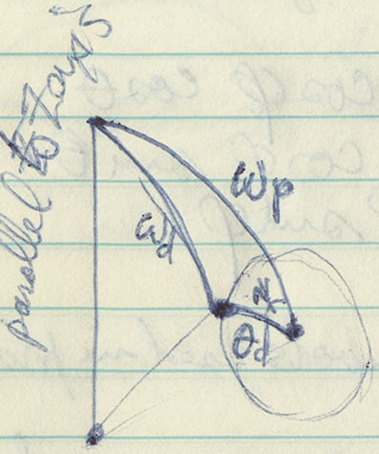
Let $\theta = 2.*\pi*\text{RAND}$

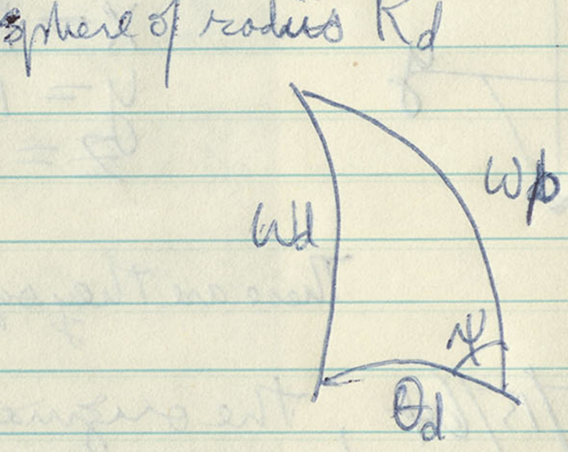
Also $\boxed{\sin\varphi \text{ uniform}}$ Let $\sin\varphi = 2.*\text{RAND} - 1.$ ← new random number for nth node

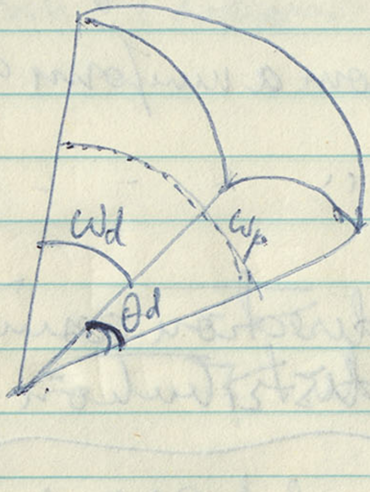
$$\alpha_n = \frac{X_n - X_p}{R_n}$$

$$\beta_n = \frac{y_n - y_p}{R_n}$$

$$\gamma_n = \frac{Z_n - Z_p}{R_n}$$



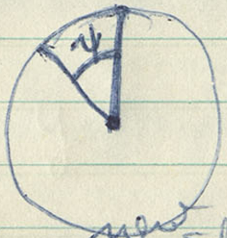




Suppose parent branch has direction cosines α_p, β_p and γ_p

~~To~~ For a given daughter, use up two degrees of freedom to get θ_d and R_d, which define a circular locus of equally probable locations for daughter node.

Let positions in this circle be represented by the angle ψ.



Let $\psi = \pi * RAND$

note, for getting new directional cosine, need only consider ψ from 0 to π.

Given γ_p calculate γ_d

Correct answer is from spherical trig.

$$\cos\omega_d = \cos\omega_p \cos\theta_d + \sin\omega_p \sin\theta_d \cos\psi$$

$$\gamma_d = \gamma_p \cos\theta_d + \sin\omega_p \sin\theta_d \cos(\pi * RAND)$$

where $\sin\omega_p = +\sqrt{1-(\gamma_p)^2}$

Alternatively, same thing could be done for α_d rel to α_p or β_d rel. to β_p, but then the other two direction cosines are defined

see next page

$$a = 1 + \left(\frac{\gamma_p}{\beta_p}\right)^2$$

$$b = -2\gamma_p(\cos\theta_d - \alpha_p\alpha_d)/\beta_p^2$$

$$C = \alpha_d^2 - 1 + \left(\frac{1}{\beta_p}\right)^2(\cos\theta_d - \alpha_p\alpha_d)^2$$

Simpler if multiply each term by $(\beta_p)^2$

The two equations are:

$$\boxed{\begin{gathered}\alpha_p\alpha_d + \beta_p\beta_d + \gamma_p\gamma_d = \cos\theta_d \\ \alpha_d^2 + \beta_d^2 + \gamma_d^2 = 1\end{gathered}}$$

where θ_d is angle between daughter & parent

Suppose α_d and θ_d have been determined

Then solve 1st eqn for β_d in terms of γ_d and subst in 2nd.

ie. $$\beta_d = \frac{1}{\beta_p}\left(\cos\theta_d - \alpha_p\alpha_d - \gamma_p\gamma_d\right)$$

$$\gamma_d^2 = 1 - \alpha_d^2 - \beta_d^2$$

$$= 1 - \alpha_d^2 - \left(\frac{1}{\beta_p}\right)^2\left((\cos\theta_d - \alpha_p\alpha_d)^2 - 2(\ )\gamma_p\gamma_d + \gamma_p^2\gamma_d^2\right)$$

$$\gamma_d^2\left(1 + \frac{\gamma_p^2}{\beta_p^2}\right) - \frac{2\gamma_p}{\beta_p^2}(\cos\theta_d - \alpha_p\alpha_d)\gamma_d + \alpha_d^2 - 1 + \left(\frac{1}{\beta_p}\right)^2(\cos\theta_d - \alpha_p\alpha_d)^2 = 0$$

Quad. formula.

$$\gamma_d = \frac{+\frac{\cancel{2}\gamma_p}{\beta_p^2}(\cos\theta - \alpha_p\alpha_d) \pm \sqrt{\cancel{4}\frac{\gamma_p^2}{\beta_p^4}(\cos\theta_d - \alpha_p\alpha_d)^2 - \cancel{4}\,ac}}{\cancel{2}\left(1 + \frac{\gamma_p^2}{\beta_p^2}\right)}$$

mult by β_p^2

$$= \frac{\gamma_p(\cos\theta - \alpha_p\alpha_d)}{1 - \alpha_p^2} \pm \frac{\beta_p\sqrt{(1 - \alpha_p^2)(1 - \alpha_d^2) - (\cos\theta - \alpha_p\alpha_d)^2}}{1 - \alpha_p^2}$$

5/20/64 Stock taking.

① Have corrected randomizers for Betty Garber's program

② Noticed error ~~at~~ in WXR611C which confused JMP+10 at one point giving peculiar output for individual totals. This should be fixed. Then, should get runs for two group & maybe for one overall group.

③ Should do giant Ve runs as noted on p. 29

④ Want to write up kinetic model now

⑤ Must finish off Aitken papers soon.

⑥ Must discuss late Mitral & other cells of Gordon's records re ? simulation cf. P.93 of Book 3

Rn 64791.0647

peak $\mathcal{E} \approx 450$ with $\mathcal{J} \approx 10$

later peak $\mathcal{J} \approx 50$ with $\mathcal{E}$ down to about 12

Rn 64793.0112 & .0121

RACT = 500.

RBSQ = 1.

RBPR = 80.

QA = 15.

ROUTB = 20.

ROUTC = 5.

QB = 40.

AFPOS = .1 i.e. ($\beta = -.1$)

5/21/64

Kinetics of uniform membrane patch

$$\tau \dot{V} = I_m R_m - V + \mathcal{E}(V_\epsilon - V) - g(V - V_j)$$

where $V = V_m - E_r = V_i - V_e - E_r$

$V_\epsilon = E_\epsilon - E_r$

$V_j = E_j - E_r$ $\qquad \psi = \frac{I_m R_m}{V_\epsilon}$

divide thru by V_ϵ & let $y = \frac{V}{V_\epsilon}$ and $\beta = \frac{V_j}{V_\epsilon}$

Then

$$\boxed{① \quad \tau \dot{y} = \psi - y + \mathcal{E}(1 - y) - g(y - \beta)}$$

and current kinetic model has

$$② \quad \tau \dot{\mathcal{E}} = k_1 y^2 + k_2 y^4 - (k_3 + k_4 g)\mathcal{E}$$

$$③ \quad \tau \dot{g} = k_5(k_3 + k_4 g)\mathcal{E} - k_6 g \underset{+k_7 gV}{}$$

WXR793C

where in 5/6/64 version of WXR93C & 94C

$\mathcal{E}$ corresp to B*RACT

g " " C*QENCHA

k_1 = RACT*RBSQ ⟶ 500.

k_2 = RACT*RBFR 4×10^4

k_3 = ROUTB 20.

k_4 = QB/QA 2.667 $\frac{40}{15}$

k_5 = QA/RACT .03 $\frac{15}{500}$

k_6 = ROUTC 5.

This presumably would correspond to a shift of my E_r toward E_ϵ ←

But then anodal electrotonus is not absolutely passive & not absolutely linear

Consider programming for a study of these kinetics

Should print y, ε, g, $1+\varepsilon+g$

for Ⓐ action potential

Ⓑ for voltage clamp

see p. 44

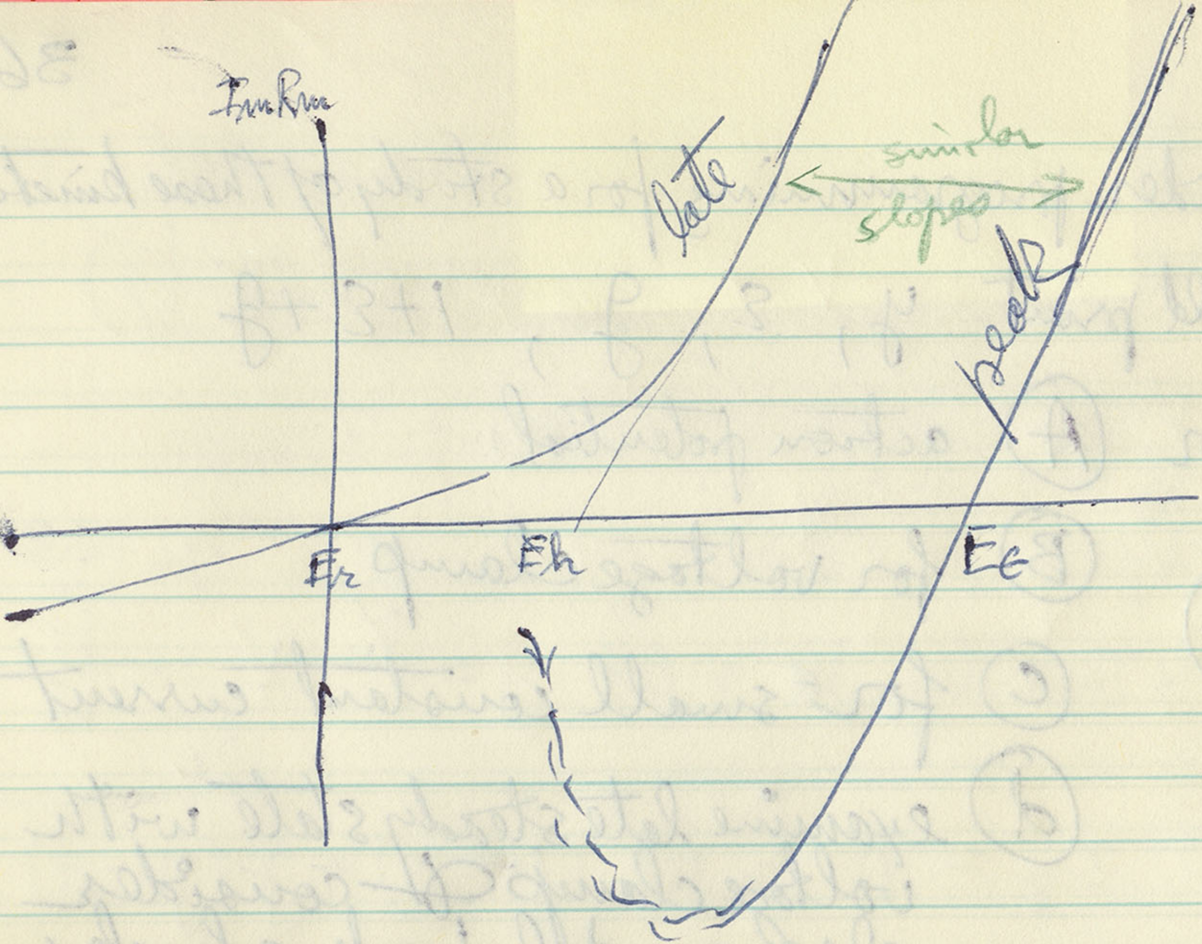
Ⓒ for small constant current

ⓓ examine late steady state with voltage clamp & consider also anodal break shocks

Problems become apparent as one tries to satisfy all these requirements with a single simplified model. But several points of interest are suggested.

① If want purely passive response to anodal stim, then must have k_1 and k_2 be zero for $y < 0$. Can do with Heaviside fcn, if desired. However, then do not get anodal break response. H&H apparently do this by swinging n and h below toward zero rest values. This I cannot do with g which is zero at rest. I could have a very small increase of ε to mimic this.

② If we wish the equations to predict st. state resp. to depol. voltage clamp, there seems



From Eq(1), for $\dot{y}=0$

$$\psi = (1+\varepsilon+g)y - \varepsilon - \beta g$$

$$= (1+\varepsilon+g)y - (\varepsilon - 0.1g)$$

intercept $\psi = 0$ $\quad y = \frac{\varepsilon - 0.1g}{1+\varepsilon+g}$ where ε & g are fcns of steady y.

~~Likely be that $(\varepsilon - 0.1g)$ becomes indept of y~~

Presumably $\frac{\varepsilon - 0.1g}{1+\varepsilon+g}$ becomes indept of y for $y \gg y_h$.

see p41

to be a problem in matching H&H concept of late g_K dominating over late g_{Na}, but maybe p. 456 of H&H paper ② wise not to assume I_{Na} makes no contribution.

In fact, it seems to me that, the late st. st. current voltage characteristic might well benefit by alternative interpretations.

i.e. if E is not negligible, then the reference point for chord conductance is not E_j but a linear combination of E_j, E_r & E_c.

To me, there has always seemed (see voltage clamp notes & manuscript re Frank, Fuortes & Nelson) to be something odd about the late st. st. I-V plot having same slope as peak plot, but with an extrap intercept near E_K. The notion that all these points are related to E_j by different chord conductances (Hagiwara & Saito) always seemed a little odd. This problem is worth looking into in present context.

It may be necessary to consider eq ④ as an alternative to eq ③

$$\boxed{④ \quad \tau \dot{J} = k_7 \mathcal{E} + k_8 J y - k_6 J}$$

this gives the desired delayed start

this permits st. st. J to remain raised with steady y even after $\mathcal{E}$ has fallen back from a peak

$$k_7 \simeq k_3 k_5 \simeq 0.6$$

$$k_8 \simeq k_4 k_5 (\text{peak } \mathcal{E}) \simeq (.08)(\overset{\sim}{450}) \simeq 36$$

Now, let us compare the late steady state of these two cases.

For equations ② & ③ when $\dot{\mathcal{E}} = 0 = \dot{J}$

we have $\frac{k_6}{k_5} J = (k_3 + k_4 J)\mathcal{E} = k_1 y^2 + k_2 y^4$
$= R(y)$

$$J = \frac{k_5}{k_6} R(y)$$

and $\mathcal{E} = \dfrac{R}{k_3 + k_4 J} = \dfrac{R}{k_3 + \frac{k_4 k_5}{k_6} R}$

$$k_5/k_6 = \frac{.03}{5.} = .006$$

$$\xi = \frac{R}{20 + 2.67j}$$

$R = 500y^2 + 4\times10^4 y^4$

$y = 0.5$

$R = 125 + 2500 = 2625$

For Eqns (2+3)

$J = 15.7$

~~$J =$~~

$$\varepsilon = \frac{2625}{20+41.9} = 42.5$$

$$\frac{\varepsilon - 0.1J}{1+\varepsilon+J} = \frac{42.5-1.57}{59.2}$$

$$\simeq \frac{40.9}{59.2} = 0.69$$

$$\Psi = (0.5)(59.2) - 40.9$$

$$= 29.6 - 40.9$$

$$= -11.3$$

Looks like ε is too large to fit desired constraints

$y = 1$

$R \simeq 4\times10^4$

$J = 2.4\times10^2 = 240$

$$\varepsilon = \frac{4\times10^4}{20+640} = \overset{60}{\cancel{58.8}}$$

$$\frac{\varepsilon - 0.1J}{1+\varepsilon+J} = \frac{58.8-24}{299.8}$$

$$\simeq \frac{34.8}{300} \simeq 0.116$$

$$\Psi \simeq 300 - 0.116 \simeq 300$$

Looks like ε is too small to fit desired constraints

Another possibility is

⑤ $\tau \dot{j} = k_5 (k_3 + k_4 j) \mathcal{E} + k_8 j y - k_6 j$

Then for st st.

$$j\left(\frac{k_6 - k_8 y}{k_5}\right) = (k_3 + k_4 j)\mathcal{E} = R(y)$$

Then $j = \left(\frac{k_5}{k_6 - k_8 y}\right) R$

$$\mathcal{E} = \frac{R}{k_3 + k_4 j}$$

But not much better

For equations ② & ④ when $\dot{\varepsilon} = 0 = \dot{j}$

from ④ $$\varepsilon = \frac{1}{k_7}(k_6 - k_8 y) j$$

from ② $$k_1 y^2 + k_2 y^4 = (k_3 + k_4 j)\left(\frac{k_6 - k_8 y}{k_7}\right) j$$

$$R = \frac{k_3}{k_7}(k_6 - k_8 y) j + \frac{k_4}{k_7}(k_6 - k_8 y) j^2$$

$$j^2 + \frac{k_3}{k_4} j - \frac{k_7}{k_4}\frac{R}{(k_6 - k_8 y)} = 0$$

$$j^2 + (7.5) j - \frac{(0.225)}{\underset{10-5y}{(5-36y)}} R = 0$$

$y = 0.5$

$$j^2 + 7.5 j - \frac{(0.225)(2625)}{\underset{7.5}{\cancel{(18-5)}}} = 0$$

approx $j^2 + 7.5 j - 80 = 0$

approx $(j + 13.3)(j - 6) = 0$

$j \simeq 6$

$\varepsilon \simeq 10 j$

$y = 1$

$$j^2 + 7.5 j - \frac{(0.225) \times 4 \times 10^4}{\underset{5}{\cancel{-31}}} = 0$$

approx $j^2 + 7.5 j - 1800 = 0$

$(j + 46.5)(j - 39) = 0$

$j \simeq 39$

$\varepsilon \simeq 10 j$

Trouble here because $k_8 y > k_6$ implies ε negative

Avoid this trouble by making $k_6 = 10$ and $k_8 = 5$

~~If $\varepsilon - 0.1g = (0.2)(1+\varepsilon+g)$~~

~~then $4\varepsilon = 1 + (1.5)g$~~

~~$\varepsilon = 0.25 + 0.375g$~~

~~$\frac{d\varepsilon}{dy} = 0.375\frac{dg}{dy}$~~

$1+\varepsilon+g = 1.25 + 1.375g$

If oversimply require (see page opposite p. 37)

$$\begin{cases} 1+\mathcal{E}+J = K \\ \mathcal{E}-0.1J = (0.2)(1+\mathcal{E}+J) = 0.2\,K \end{cases}$$ const max slope

Then can solve $\mathcal{E}+J = K-1$

$\mathcal{E}-0.1J = 0.2K$

to get $$\boxed{\begin{aligned} J &\simeq 0.73K-0.91 \\ \mathcal{E} &\simeq 0.273K-0.091 \end{aligned}}$$

Which is obviously too simple to serve the purpose. for all $y>y_u$

However, more generally, $\mathcal{E}$ & J are fcns of y
st.st. clamped

and $$\frac{dY}{dy} = (1+\mathcal{E}+J) + \left(\frac{d\mathcal{E}}{dy}+\frac{dJ}{dy}\right)y - \frac{d\mathcal{E}}{dy} - \beta\frac{dJ}{dy}$$

$$= 1+\mathcal{E}+J+(y-1)\frac{d\mathcal{E}}{dy}+(y-\beta)\frac{dJ}{dy}$$

$$\simeq K \text{ for } y > y_u$$

~~also $1+\mathcal{E}+J \approx 5(\mathcal{E}+\beta J)$ or $\mathcal{E} = \frac{1+(1-5\beta)J}{4}$~~

~~$\therefore\ K \approx 5(\mathcal{E}+\beta J)+(y-1)\frac{d\mathcal{E}}{dy}+(y-\beta)\frac{dJ}{dy}$~~

~~$\approx 1.25+1.375J+\left[(y-1)(0.375)+(y-\beta)\right]\frac{dJ}{dy}$~~

~~$\approx 1.25+1.375J+(2y-0.275)\frac{dJ}{dy}$~~

May resolve by noting that ⟶
this "late" curve does not corresp to
a true st. st. but more nearly to
a peak J current. Check this out
with my model.

for y from 0.6 to 1.5 range
Would like

$$\frac{dJ}{dy}(y+0.1) + \frac{d\mathcal{E}}{dy}(y-1) \simeq 99 - \mathcal{E} - J$$

↑
.7 to 1.6   -.4 to +.5

Consider

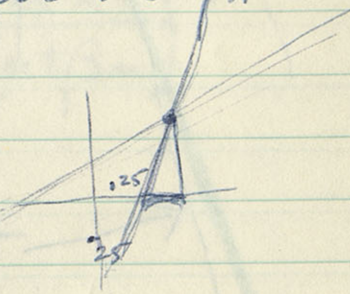
$$Jy + 0.1J + \mathcal{E}y - \mathcal{E} - 99y = \text{const.}$$

diff. with respect to y gives above.

5/22/64

The H&H approach was to assume late G due to G_K and match G_K st st as a fcn of V to the data.

Here, the attempt has been to see if could get reasonable volt. clamp st st. on the assumptions that both $\mathcal{E}$ & $\mathcal{J}$ contribute. But first attempt has not worked out.



for H&H data, $K \approx 100$

$y_h \approx 0.25$

would imply that $\psi_{\text{intercept}} \approx -25$

this would imply $\mathcal{E} - 0.1\mathcal{J} = 25$

Note st. st. $\mathcal{E}$ & st. st. $\mathcal{J}$ would be fcn of y

for any given $y_1 \gtrsim 0.6$ we can only say that $\psi_1 \approx 100(y_1 - .25)$

$y_1 = \frac{\psi_1}{100} + .25$

$$\left.\begin{aligned} \text{Thus } \psi_1 = 100(y_1 - .25) &\simeq (1+\mathcal{E}_1+\mathcal{J}_1)y_1 - (\mathcal{E}_1 - 0.1\mathcal{J}_1) \\ \text{and } \psi_2 = 100(y_2 - .25) &\simeq (1+\mathcal{E}_2+\mathcal{J}_2)y_2 - (\mathcal{E}_2 - 0.1\mathcal{J}_2) \end{aligned}\right\}$$

It is not true in general, that $1+\mathcal{E}+\mathcal{J} = 100$ and that $\mathcal{E} - 0.1\mathcal{J} = 25$
if it were, $\mathcal{E}$ & $\mathcal{J}$ would have fixed values as ~~in~~ the upper half of p. 41

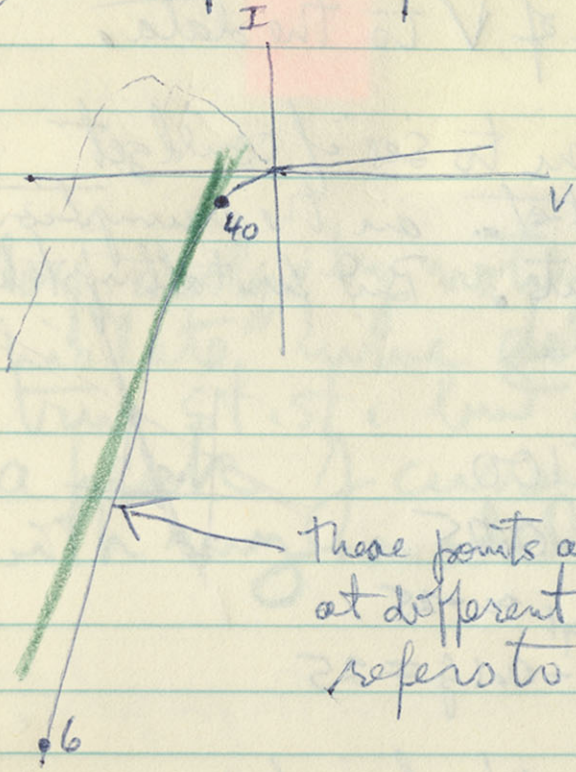
But for $y_1 > 0.6$, we say that $\frac{d\psi}{dy} \simeq 100$

$$\frac{d\psi}{dy} = 1 + \mathcal{E} + \mathcal{J} + (y-1)\frac{d\mathcal{E}}{dy} + (y+0.1)\frac{d\mathcal{J}}{dy} \simeq 100$$

For very rough approx, assume $\frac{d\mathcal{E}}{dy}$ negligible

$$\text{then } (y+0.1)\frac{d\mathcal{J}}{dy} + \mathcal{J} \simeq 100 - 1 - \mathcal{E} = 99 - \mathcal{E}$$

Fig. 13 cmp. 439 of H, H&K



These points are labeled as having been obtained at different points in time, and text refers to a "steady state"

ranging from 6 msec to 40 msec

because peaks earlier

because slow approach

If all were taken at same time, say 10 or 15 sec, the top bend would go straighter to an intercept and the bottom points would shift up.

5/22/64

Relaxation conclusion this afternoon is that not likely to get st. st. with my simple model. After all, in H&H paper five, their relation which would corresp roughly to my J vs y sought, is

$$\frac{g_{K\infty}}{g_{K_{max}}} = \left(n_{\infty}\right)^4 = \left(\frac{\alpha_n}{\alpha_n+\beta_n}\right)^4$$

where $\alpha_n = \dfrac{0.01\,(V+10)}{\exp(0.1(V+10))\ -1}$

and $\beta = 0.125\ \exp(V/80)$

(p. 510 & 511 of paper ⑤)

However, note that H&H do not fit a true experimental steady state themselves;

They seem to use a peak K current, the late conductance curve would look different if all points were obtained for the same time value in the voltage clamping transients.

See left page

∴ attempt of previous pages was too severe.

The suspicion I wish to check is that peak K current corresp to a significantly non-zero $\mathcal{E}$ and that, perhaps, the value of $\boxed{\dfrac{\mathcal{E} - 0.1J}{1+\mathcal{E}+J}}$ is similar for all $V > V_h$ as this peak time.

5/25/64 – 5/27/64

Wrote WXR 751C

with the intention of checking my kinetics against the experimental constraints. At first, simply print out values as they are computed. Later possibly add plot.

Print KT, TK, C, P, V, E, Q, G

working values

Z

A

X

Y

where C = current as $\psi = \frac{I_m R_m}{E_e - E_r}$

P = passive $\frac{V_m - E_r}{E_e - E_r}$

V = non-passive "

E = ε

Q = g

G = $1. + \varepsilon + g$

KHVSD (Heaviside) = { 1 means suppress neg V contribution to $\dot{\varepsilon}$
{ 0 " include " " " "

KLAMP = { +1 means voltage clamp
{ 0 means zero current
{ −1 means non-zero current clamp

rate constants R(K) for K=1,7

All time expressed as $T = t/\tau$ (i.e. DT, TK, DELT, $\frac{\partial V}{\partial T} = \tau \dot{V}$ etc.

DX = EGRO − ELOSS = R(1)*ASQ + R(2)*AFR − (R(3) + R(4)*Y)*X

DY = QGRO − QLOSS = R(5)*ELOSS + R(7)*A*Y − R(6)*Y

KLAMP≤0 [DA = C − A + X*(1.−A) − Y*(A+.1)
DZ = C − Z corrected 5/28/64

KLAMP=1 [C = V − E*(1.−V) + Q*(V+.1)

5/28/64

first test of WXR751C

results encouraging: caught error in P

In these tests peak $\mathcal{E}$ was ≈ 640 } factor of 10
peak g was ≈ 55

whereas in H&H, factor is less than 3

Their peak g_{Na} corresp $\approx$ to $\mathcal{E} = 300$
g_K ~ ~ ~ ~ $g = 120$

This is based on $g_{rest} \approx 0.1$ for their curves.

~~However, their st. state $g_{Na\infty} \approx 20$ m℧/cm²~~

for clamping at equilib pot, their $g_{Na\infty} \approx 40 \longrightarrow \mathcal{E} \approx 400$
$g_K \approx 20 \longrightarrow g \approx 200$

Because of this decided to try larger R_5
also add R_7

Next test has two series

	R_1	R_2	R_3	R_4	R_5	R_6	R_7
1st Series	500.	4×10^4	20.	2.7	.03	5.	0.
2nd Series	"	"	"	3.	.1	5.	2.5

6/2/64 2nd Series went too far in this direction.
Q blew up > 500

2nd Series

		C		E		g	
.9	.01	-19.7		236		2.9	
			>500			>5000	
.7	.03	-44.		179		11.3	
			227		11.2		287
.5	.05	-30.		68		5.9	
			35.3		11.8		67.7
.3	.09	-8.8		13.9		1.7	
			-1.97		8.11		8.5

note nearly equal

6/3/64

Analysis of 6/2/64 results with WXR 751C

During Spike

1st Series peak $\mathcal{E} \simeq 650$ peak $J \simeq 55$

with $J = 15$

at .01 τ after peak V

2nd Series peak $\mathcal{E} \simeq 350$ peak $J \simeq 87$

with $J = 20$

at peak of V

Voltage clamping

1st Series

V	TK	C	$\mathcal{E}$	J	
.9	peak = .03	-43.4	523	7.9	
	final = .9	153	60		158
.8	peak .05	-71.2	257	6.5	
	final	31	56		58
.5	.08	-42.8	90	3.1	
		-11.4	43		16
.3	.15	-10.8	16.3	.9	
		-8.8	14		2

because R_7 tends to enhance J most when V is large. →

∴ New values will be $R_6 = 10.$ (twice previous)
requiring $R_5 = 0.1$
together! " $R_3 = 100.$

Try $R_4 = \{ 1.$ and $100.$

Leave R_1 & R_2 unchanged; $R_7 = 0$

Note that $R_4 = 100$ holds E_{ss} to $\frac{J_{ss}}{1+J_{ss}} < 1$

or more generally, if $R_3 = R_6/R_5$, $\boxed{E_{ss} = \frac{J_{ss}}{1+\frac{R_4}{R_3}J_{ss}}}$ $\frac{E_{ss}}{J_{ss}} = \frac{1}{1+\frac{R_4}{R_3}J_{ss}}$

late steady state.

Problem is to decrease $\mathcal{E}$ below J for small V & J.

Also, second series got J too big.

∴ R_7 is really not helpful. Eliminate R_7

Aim to juggle rate constants to reduce $\mathcal{E}$ & increase J in spike and in voltage clamp.

^ to get G time course correct.

→ Increase R_6 because J decays too slowly

$$J_{ss} = \frac{R_5}{R_6}\left(R_1V^2 + R_2V^4\right)$$

$$\mathcal{E}_{ss} = \frac{R_1V^2 + R_2V^4}{R_3 + R_4J_{ss}} = \frac{(R_6/R_5)\,J_{ss}}{R_3 + R_4J_{ss}}$$

∴ for J_{ss} very large, $\mathcal{E}_{ss} \longrightarrow \frac{R_6}{R_4R_5}$

for J_{ss} very small, $\mathcal{E}_{ss} \longrightarrow \frac{R_6}{R_3R_5}J_{ss}$

In order that $\mathcal{E}_{ss} < J_{ss}$ for small J_{ss}, need $\boxed{\frac{R_6}{R_3R_5} \lesssim 1}$

for $V=1$, $J_{ss} = \frac{R_5}{R_6}(R_1+R_2) \approx 4\times10^4\left(\frac{R_5}{R_6}\right)$

∴ if want J_{ss} around 400, need $\frac{R_5}{R_6} \approx 10^{-2}$

∴ need $R_3 \approx 10^2$ to satisfy

R_4 has some freedom; it will affect spike & slope of $\mathcal{E}_{ss}$ vs V

for third series. $TK \simeq .07$, $R_3 = 100$ get $\simeq 300(1-.7) \simeq 90$

$C \simeq 0.7-(0.3)90) \simeq -27$

for second series ε^*

Provided that the transients are not ruined, previous pages show that $\mathcal{E}_{ss}$ can be held down according to

$$\boxed{\mathcal{E}_{ss} = \frac{\left(\frac{R_6}{R_3 R_5}\right) J_{ss}}{1 + \frac{R_4}{R_3} J_{ss}}}$$

in particular, if $R_3 = R_4 = \frac{R_6}{R_5}$, $\mathcal{E}_{ss} < 1$

more generally, whatever R_4 may be, if $R_3 = \frac{R_6}{R_5}$, $\mathcal{E}_{ss} < J_{ss}$

∴ May possibly need to slow everything down.

If we desire $\mathcal{E}_{ss} < \alpha J_{ss}$

then require $\frac{R_6}{R_3 R_5} = \alpha$

Look at C for V = .7 & see if can estimate peak C.

1st approx would be for $J = 0$ & guessed TK

$V^2 = .49$

$V^4 \simeq .25$

$$\mathcal{E}^* \approx (\tau \dot{\mathcal{E}})(TK) \approx (TK)(10^4)$$

for TK = .03, est. $\mathcal{E} \simeq 300$

Better approx is This $- \frac{k_3 (TK)(\text{This})}{3}$

i.e. $\mathcal{E}^* \simeq (TK)(10^4)\left(1 - \frac{k_3 TK}{3}\right)$

e.g. $\approx 300(1 - .2) \approx 240$

$$C \approx V + \mathcal{E}^*(1-V) \approx 0.7 + (0.3)\mathcal{E}^* \approx 72$$ ✓

for first series.

6/4/64 – 6/5/64 Series 3, 4, 5, 6, 7, 8 of WXR751C were run and compared, including also 1 & 2

General: In ② spike falls faster than rise (∴ ruled out)
In ③, ⑥, ⑧ fall very similar to rise (∴ ruled out)
In ④ overquenched (∴ ruled out)
This leaves
①, ⑤ & ⑦ all look "physiological" because rise is fast & fall is slower than rise

Series ① shows more rounded top, probably because of smallest R_3 and R_5 gave smallest ratio of J_{peak} to E_{peak}

Note that largest ratio of J peak to E peak occured in
series ③ with ratio $>$ 1/3
while series ⑧ $=$ 1/3
& series ⑥ $\simeq$ 1/3
all these tend to fall too fast.

Comparing ①, ⑤ & ⑦, perhaps ⑤ is prettiest, but 7 & 1 are OK.

Note that ① corresponds to the extracellular calcs done earlier with WXR 793C

⑦ is similar, but R_6 is doubled, R_3 is 2.5 times

→ This seems to give more realistic J decay rate, but this may have to be tested in terms of refractory period (i.e. blocks & reflections)

For extracellular study & such applications, need to consider differences of these cases with regard to axon-soma block & synaptic threshold.

For near threshold conditions, there may be a significant difference in the steady J_{ss} which would increase threshold.

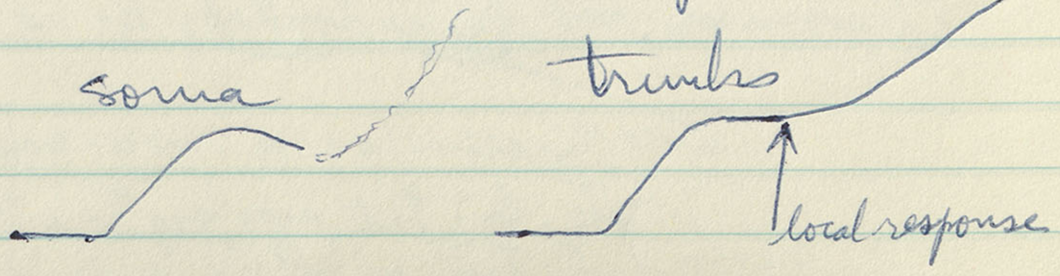
i.e. just subthreshold, one would reach a near steady state where $\frac{dE}{dt} = 0 = \frac{dJ}{dt} = 0 = \frac{dV}{dt}$

Then $J_{ss} = \frac{R_5}{R_6}\left(R_1 V^2 + R_2 V^4\right)$

also $E_{ss} = \frac{R_1 V^2 + R_2 V^4}{R_3 + R_4 J_{ss}} = \frac{(R_6/R_5) J_{ss}}{R_3 + R_4 J_{ss}}$

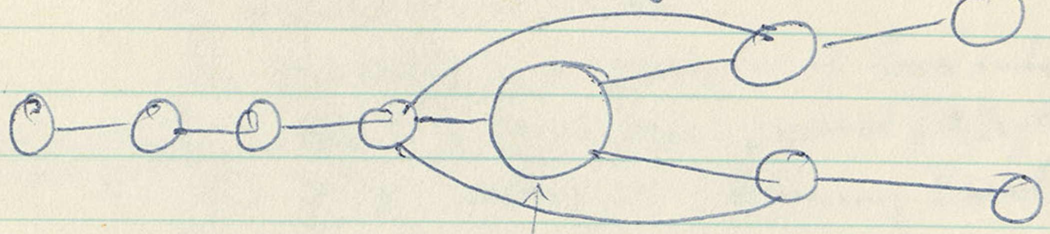
Easiest trick to raise soma threshold is to put a factor such as 0.8 in front of E in the expression for $\dot{V}$ at the soma

An AB break will occur when the dendritic trunks nearly fail to fire, so that the soma transient starts to decay before the trunks enter local response and takeoff.

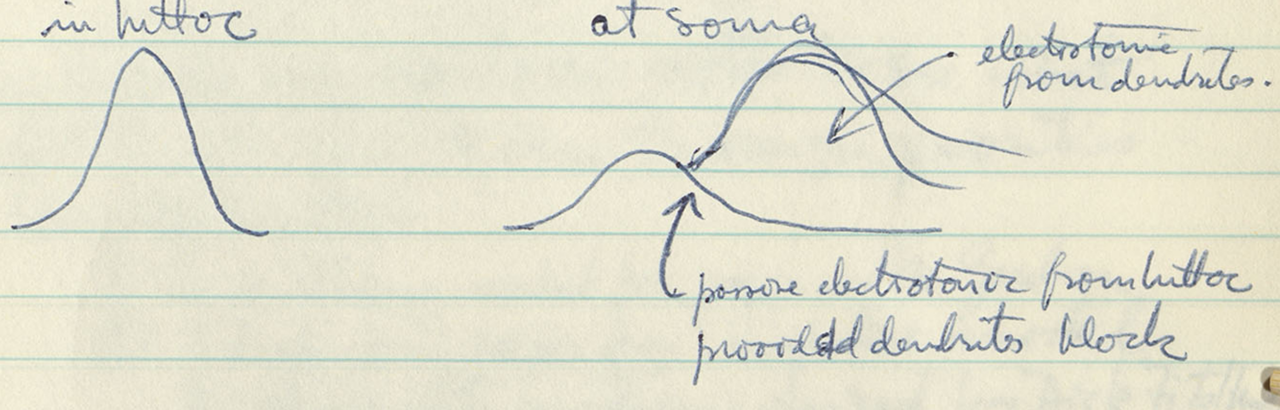


6/6/64

Thoughts about simulating AB break & block



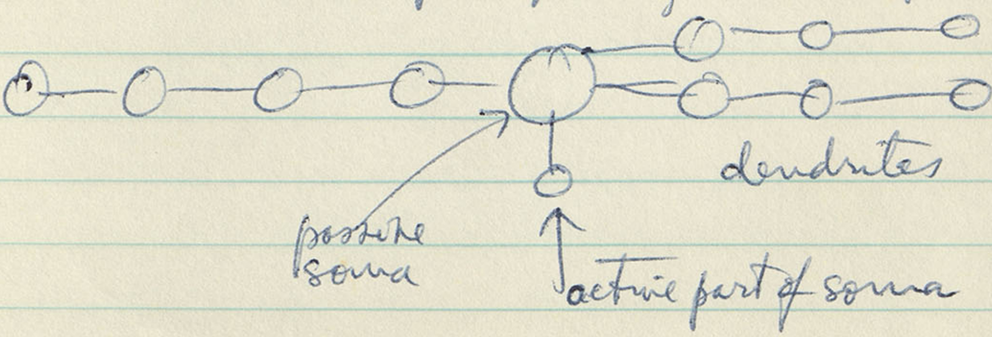
a possible higher threshold passive soma with active dendrites could give A, AB



Or possibly soma need not be passive, provided that it has a higher threshold such that dendrites fire before soma, to give AB break

This could be managed either by having higher soma threshold,

or perhaps by dendritic facilitation



6/10/64 — 8/12/64

Major interruption of research

A. one week in Texas

B. one week here taking care of loose ends & thinking about Canberra paper, reviewed FitzHugh paper.

also Jean Altman's medical & job situation

C. 3 1/2 weeks at Bethany Beach

D. one week picking up loose ends, reviewing things for Marsan, etc. also cars.

also Garber trees

E. one week to complete Canberra paper which was dittoed & sent off 8/11/64.

Today looking over old loose notes to see what needs to go in here & also to assign priorities for coming month.

① Computations needed for paper with Gordon

② Rough out paper on impulse model & check into questions raised by Dick FitzHugh (see next page for notes from 6/18/64)

③ AB break p. 51

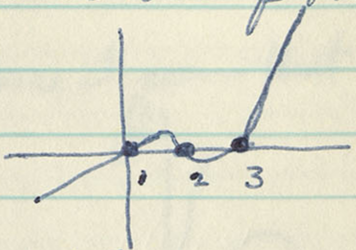
④ Refer back to p. 34 & p. 5 & p. 30

8/14/64 put pictures up on office wall

8/12/64 copy of notes dated 6/18/64 after showing Dick FitzHugh the results of WXR751 (see p. 49)

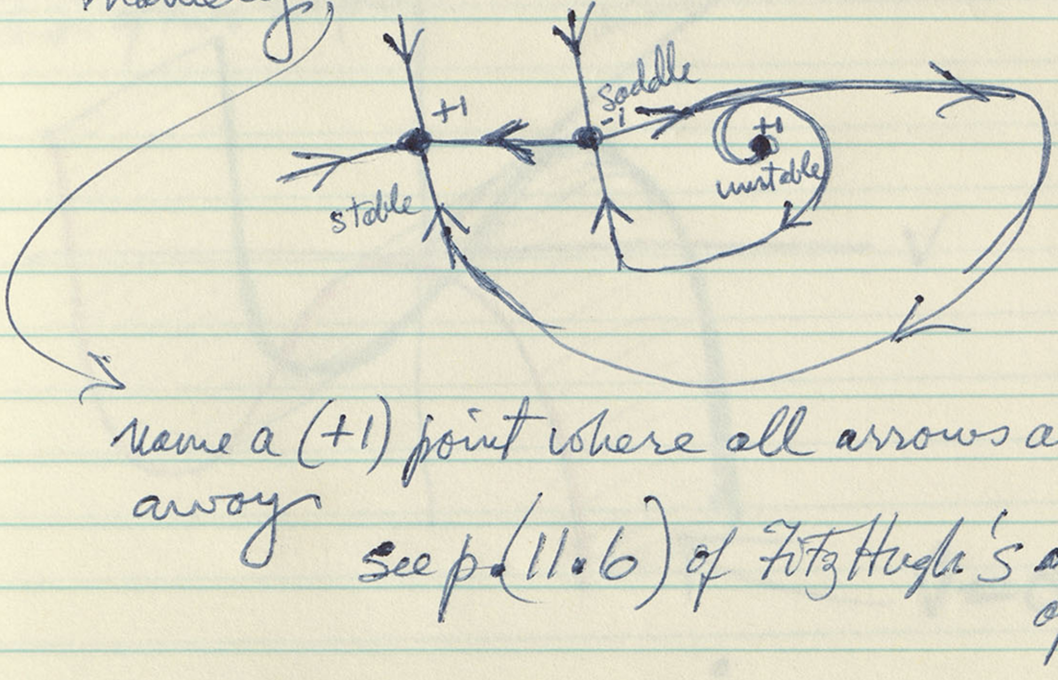
Dick had two suggestions:

① Compute Ess and Jss for small V, and then compute and plot I vs V curve to see if there are three singular points, as implied by my crossover point away from origin.



If so, want to investigate stability properties of the third point. It would be awkward if this were stable, because then would have ~~two~~ stable resting potentials.

However, Dick says it could be unstable in a special way which he has not met before, namely,

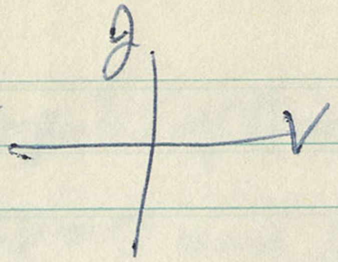


name a (+1) point where all arrows are directed away

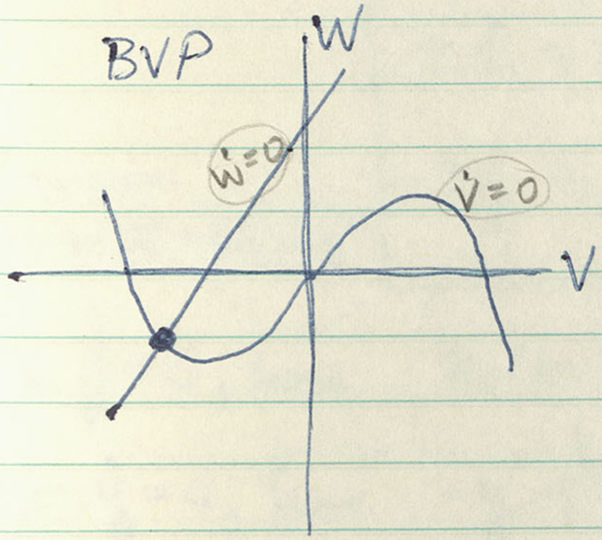
See p. (11.6) of FitzHugh's manuscript appendix

If I really have such a point, he would be quite interested.

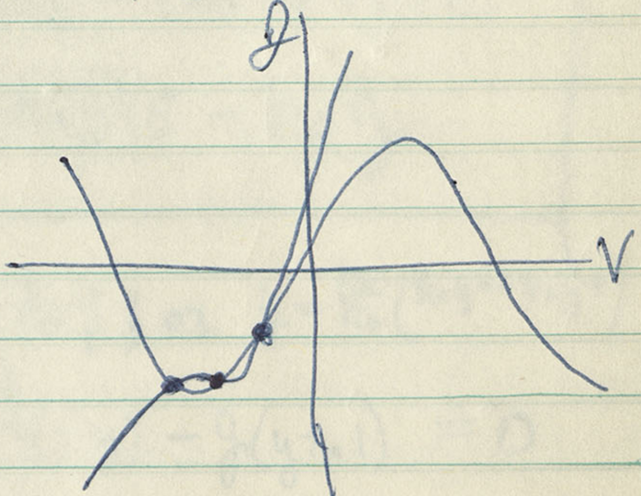
Also, plot



for $\mathcal{E}$ constant at st. st. value, to get nearest approx to BVP model.

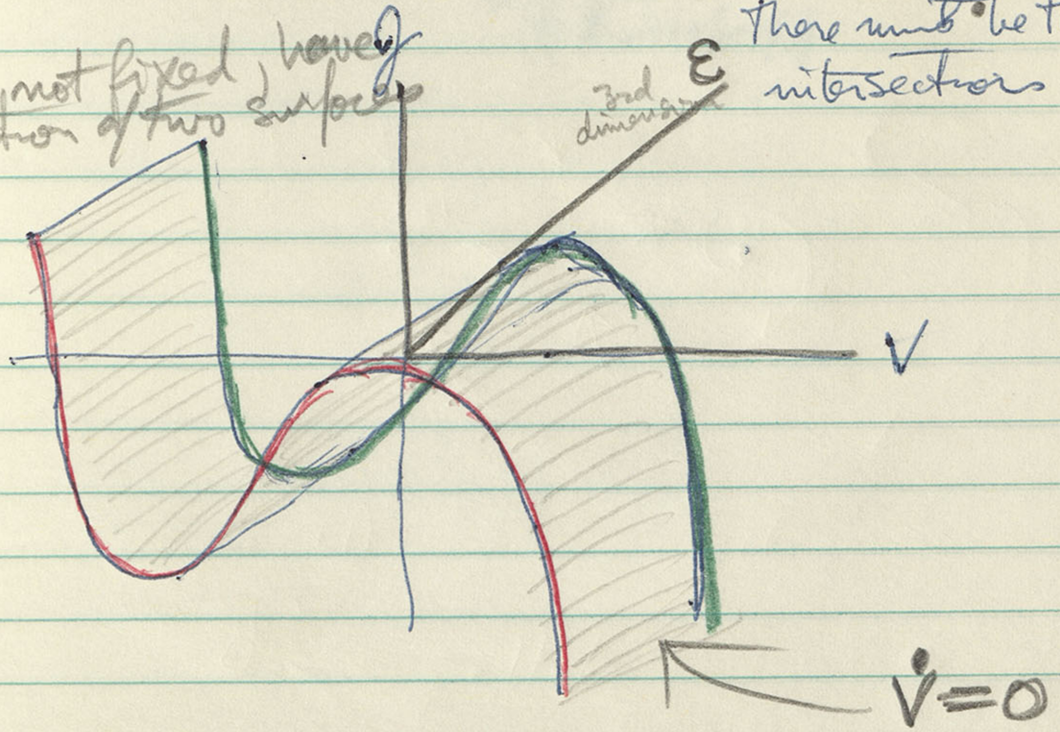


Here it seems that



There must? be three intersections here also.

For $\mathcal{E}$ not fixed, have intersection of two surfaces



Intersects with surface, $\dot{j}=0$

Refer back to page 35 of this book, where $y = \frac{V_m - E_r}{E_e - E_r}$

Also, set $\psi = 0$ and $\beta = -0.1$

Then

$$\boxed{\begin{aligned} \tau \dot{y} &= -y + \varepsilon(1-y) - g(y+.1) \\ \tau \dot{\varepsilon} &= k_1 y^2 + k_2 y^4 - (k_3 + k_4 g)\varepsilon \\ \tau \dot{g} &= k_5(k_3 + k_4 g)\varepsilon - k_6 g \end{aligned}}$$

$\dot{\varepsilon} = 0$ gives $(k_3 + k_4 g)\varepsilon = k_1 y^2 + k_2 y^4$

for $\dot{g} = 0$, have $k_5(k_3 + k_4 g)\varepsilon = k_6 g$; or $g = \frac{k_5}{k_6}(k_1 y^2 + k_2 y^4)$

for $\dot{y} = 0$, have $-y + \underbrace{\left(\frac{k_1 y^2 + k_2 y^4}{k_3 + k_4 g}\right)}_{\text{st. st. value of } \varepsilon \text{, as a fcn of } g}(1-y) - g(y+.1) = 0$

8/22/64 Got Dorothy to run off old dittos of Spherical Neuron Field paper & preparation to completion of same.

8/24/64 Discussed late potential of Olfactory Bulb field potentials with Gordon today. (See next page)
We had plotted the theoretical iso contours (vs depth & time) on Friday. Now, analysing to see what ought to be checked out next.

The ones plotted were 64791.0666 passive dendrites {hot kinetics
and 64791.0669 active dendrites {cool kinetics

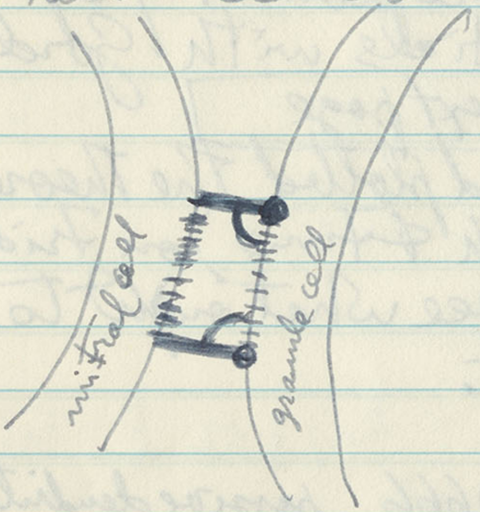
Question was raised whether secondary dendrites should be treated separately because of

ⓐ they contribute differently to extracellular pot because λ vs depth is different, even for antidromic. This may smear after positivity, even for active dendrites.

ⓑ possibility of different synaptic activity

I

The resting state of plaque could be like a low resistance electrical synapse.

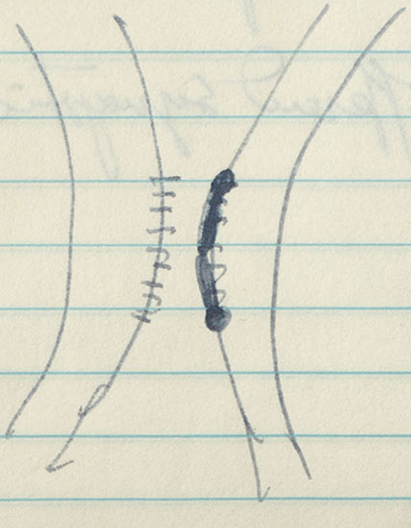


The hatched membrane has high conductance e.g. high K^+ permeability from one cell to the other, in both directions

For mitral cell depol to have depol. effect on granule cell, e.g. K^+ would flow from m. to g.

II

Sufficient summation or regeneration of ~~mitra~~ granule cell depolarization causes a change which exposes the mitral cell K^+ plaque to the extracellular medium, causing inhibition.



As though hinged gates have swung from mitral contact to granule contact.

In effect, this would prevent K^+ back flow from g. to m. + block m. near rest.

8/24/64

Thoughts about dendro-dendritic synapses between granule cells & mitral cells of olfactory bulb.

① The late potential is a dipole with zero contour at mitral soma layer, neg peak in external plexiform layer & pos. peak in internal plexiform layer. Seems to best fit granule cells, because I feel that such a symmetric dipole depends upon a substantial core conductor which extends from the neg. to pos. peak. also

② This epoch is associated with mitral cell inhibition. ∴ the other, but remoter possibility is an active hyperpol. being caused at mitral axon hillock

Here is a model whereby dendro-dendritic contacts between mitral cells and granule cells could account for these phenomena. Formally, activation of the mitral cell (either anti- or orthodromic) will depolarize its secondary dendrites; these could, by dendro-dendritic placques, depolarize the granule cell dendrites; if the granule cell depolarization reaches some threshold, then the placques change to have

or collaterals could do this

? perhaps due to regenerative depolarization

an inhibitory effect upon the mitral cells. The regenerative depolarization of the granule cells would set up the prolonged dipole field that is recorded. The granule cell has no axon & ∴ may have no prop. spike. This inhibition would fun as "lateral" or "surround" inhibition and should serve to sharpen contrast.

For #⑤ of p. 49   cf. page 35 ↓

$R_1 = 500$ ⟶ RACT = 500

$R_2 = 4 \times 10^4$ RBSQ = 1. ; RBFR = 80.

$R_3 = 50$ ROUTB = 50.

$R_4 = 1.$

$R_5 = .05$

$R_6 = 10.$ ROUTC = 10

$$QENCHA = R_5 * RACT = \frac{500}{20} = 25$$

$$QENCHB = R_4 * QENCHA = 25$$

∴ Try	Cool	Hot
RACT	400.	600.
RBSQ	1.	1.
RBFR	80.	80.
QENCHA	20.	30.
ROUTB	50.	50.
ROUTC ~~QENCHB~~	10.	10.
QENCHB	20.	30.
AFP8S.	10.	10.

8/25/64 Because 64791.0666 (passive dendrites
hot kinetics)

used dendritic ε in order to avoid delayed or blocked soma spike, it is not possible to run the equivalent problem for active dendrites. Geometric handicap: $\frac{USD}{USA} = 80.$

∴ Decided to try to reduce geometric handicap to a value of 40. and try to manage without dendritic ε.

(see p.15 of this book)

Also, now using WXR793C (although 791 still avail) and consider that $\dot{V} \propto RBSQ*V^2 + RBFR*V^4 + \cdots$ whereas in WXR791C we have $\dot{V} \propto RINB*V^3$

∴ Set up 64793.8100 series for new cool kinetics with $L/\lambda = .8$

and 64793.8800 series for new hot kinetics with $L/\lambda = .4$

	UA	UD	USA	USD	NSD	DZ
for 8100 series.	25.	100.	2.	80.	8	.1
for 8800 series	100.	400.	2.	80.	8	.05

Here the UD values = $\left(\frac{1}{DZ}\right)^2$, as they should

$UA = \frac{1}{4} UD$ to take care of diameter for same ΔL

8/26/64

dendritic I.C.

64793.8101 axonal spike fine : blocked at soma I 0.
(active & passive very close)

64793.8102 " again .05

This consumed checkout 5 minutes. IPAB = 0
NT * NSTEP = 404

8/27/64

cool kinetics, dendritic I.C. = 0.1

64793.8103 soma block with passive dendrites
barely above threshold with active dendrites

64793.8801 – 8804 all blew up because NSTEP was too small for hot kinetics

64793.8104 I.C. = .15 soma block with passive dendrites (peak = 0.1590)
soma invaded with active dendrites
axon had a reflected orthodromic
presumably because of soma delay.

64793.8105 I.C. = 0.2 soma block with passive dendrites (peak = 0.2113)
synchronous soma-dendritic → soma invaded with less delay (active dendrites)
in this case there is no reflection in axon.

64793.8805 did not have an axonal spike.
These kinetics (hot) were ~~presumably overquenched~~

Also 64793.8811 8/28/64 Due to UA = 100 implying $\Delta Z_A = 0.1$
Example of Rushton's critical length requirement

8/28/64

64793.8812 UA still 100. implying $\Delta Z_a = 0.1$

I.C. = 0.4 in ① and ②

even so, axon still failed to fire.

64793.8813 same with I.C. = 0.8 in ① only

Here axon did fire, but soma blocked.

even though dendritic I.C. = 0.05

Now reduce UA = 50., VD = 200. $\frac{USD}{USA} = 40$

DZ = 0.0707

RACT = 600.

QA = QB = 30.

Also Giant Extracellulars

64793.8814 dendritic I.C. = 0.1

Got long axon-soma delay

beginning of synchronous dendritic spike

64793.8815 dendritic I.C. = 0.2

axon soma delay .07τ

Good Soma spike, except possibly falls too fast, may wish to reduce quench

* Dendritic Spike synchronous

Good when wish to show how this reduces extracellular.

Good Giant Spike $\begin{cases} \beta = 100, 25 \\ \gamma = 1, 1 \end{cases}$

8/27/64 – 8/28/64   UA = 25.   UD = 100. $\frac{USD}{USA} = 40.$ 61

64793.8104   Cool (RACT = 400.   quench = 20.)

Dendritic I.C. = 0.15   IFAB = 0

Got delayed soma spike for active case (queer reflection)
" blocked "   passive

64793.8105   Dendritic I.C. = 0.2

Active Dendrites fired 0.02τ ahead of soma; almost synchronous

Soma blocked in case of passive dendrites, although soma peak = 0.2113
must be near threshold.

64793.8201   Dendritic Synaptic ε

Also $\frac{USD}{USA} = \frac{1}{4}$ to make axon mimic load due to secondary dendrites of mitral cell

USD = UD

Discovered program problem of some undefined dendritic J.
This difficulty removed by WXR794C

* Successfully caused soma to fire inspite of secondary dendritic load. Soma + ~~[illegible]~~ secondary spike was synchronous
but note that secondaries active like soma

RACT = 400.   quench = 20.

* Sharp falling phase of soma spike is responsible for pos. peak of extracellular

Note: for extracellular potentials of population. May need to compute some spatial and temporal smear.

also, firing & non firing smear

May need to invoke radial V_e to get deep pos. but I believe it can be gotten also by placing E farther out in dendrites.

8/28/64 – 8/29/64

64793.8202 similar to 8201, except only 6 dendritic cpts.

Put ε = 8. in two most peripheral cpts.
Put J = 8. in two trunk cpts.

Soma and secondaries fired at very end, after the inhibition had been turned off.

At peak of dendritic Epsp (i.e. KT = 40), for KVE = 2 (i.e. shunt external)

Get Neg Ve in cpts 9 & 10
pos Ve for the rest.

But this is not yet a good model for granule cell because of the heavy axonal (2ndary dendritic) load

64793.8203 VA = UD = USA = USD = 25.

This is granule cell equivalent cylinder
Put ε = 1.0 in dendritic trunks (5 & 6)
also RACT = 100. and quench = 10.

passive synaptic potential starts out spatially symmetric
However, asymmetry develops, presumably because of local response in ~~[illegible]~~ compartments 1–4.

(cpt 5 & 6 most neg.)

for KVE = 1, all cpts are neg. except cpt. 10 at zero
for KVE = 2, (cpts 5 & 6 most neg.) ; cpt 10 went slightly +

For granule cell, need deep source, ~~[illegible]~~ to make deep pos.

8/31/64 WXR794C

revision of WXR 793C

Increased dimensions of BEB (JZ, KEJ) and BJC (JZ, KEJ) to (14,10)

and arranged to read in from separate cards 966 format which include all compartments for E & J at 2453

Also, ~~at~~ after 382 AB(JZ) = AB(JZ) + BEB(JZ, KEJ)
AC(JZ) = AC(JZ) + BJC(JZ, KEJ)

9/1/64 corrected this DO Loop 384 JZ=1,NZ @ 380

This means that E & J are added to existing values at KTA, and nothing is done at KTB in the active case, whereas E & J are set to zero in the passive case, but not in the axon and soma.

At 725 arranged a test such that

IFVE = 1 skips printing out case of KVE = 1 and gives only KVE = 2.

whereas IFVE = 2 or greater gives KVE = 1 and KVE = 2

i.e. only with external shunt.

Note: to mimic radial effect on deep re, could make CORE > 1.

8/31/64

64793.8816 dendritic I.C. = .2, .2, .15, .10, .05, .0

otherwise like .8815 on p. 60

Here attempted make ~~some~~ dendritic spike less synchronous.

Got long axon-soma delay ≈ .25 τ
and it looks as though dendrites would be synch.

64793.8817 Reduced quench from 30. to 20.
and ROUTB from 50. to 40.
Also added a third giant. β = 6.2
proved too large for Gordon

dendritic I.C. = .25, .20, .15, .10, .05, .0

axon-soma delay ≈ 0.18 τ & got reflected ortho.
dendritic spike almost synchronous.

64793.8818 same except I.C. = .25 in all dendritic cpts.

obviously underquenched.

8817 had interesting spike shape, but probably fall too slow.

better in 8819 where quench was increased back up to 25. (see next page)

9/1/64

64793.8819   quench = 25.   ROUTB = 40.

dendritic I.C. = .30, .30, .20, .20, .10, .10

IFAB = 0

Good run: for active dendrites { axon soma delay = $.07\tau$
synchronous dendritic spike

Shape of action potential very good

for passive dendrite: axon soma delay = $.19\tau$
reflected orthodromic

Good giant extracellulars

This series has shown that for active dendrites $6\times(\Delta Z = .071)$
$Z \approx .42$
it is almost impossible to avoid synchronous dendritic spike.

If this wipes out extracellular (must now be run) this may provide a strong argument against active dendrites, contingent upon Z length.

Note that 64791.0669 had $Z = 5\times(.25) = 1.25$

Also, AB story may need somatic inhibition and perhaps USA larger. Note that soma has disadvantage rel. to active dendrites because it is yanked down by hillock after pos. Maybe hillock should be cooler.

9/1/64 64794.8204 first test of new program.
mimic granule cell.

Results even where zero
Program fault at statement 380

64794.8205 had same trouble & lead to discovery of problem

Now put in a recompile.

Reran 64794.8205 started but blew up because
NSTEP = 10 too small for DT = .05

Put back as .8206 with NSTEP = 20

64793.8820 worked very well
quench = 25. ROUTC = 40.
I.C. = 0.3 at soma & dendritic trunks

Both Active & Passive were good.
Except active had too little axon soma delay

Set up Production runs (9/3/64) NT=51, DZ = .1, NJD=8, NJG=2
.8821 similar to 8820 with IPAB = +1
.8822 . . . . . 8819 . . . −1
initial conditions

actually not consistent with
UD = 200.

Continued on p. 74

64794.8206 attempt at granule cell with all $\mu = 25$.

Results suggestive, but DT = .05 too large
also RACT = 200. too large
for $\varepsilon = 4$.
got pseudospike at KT = 2

∴ set up 8207 with DT = .02, NSTEP = 10
deleted I.C,
reduced RACT to 100.
also ROUTB to 10.
and ROUTC to 5.
& ε (dendritic to 2.
J to 1.

64794.8207 ↗ This was still too hot & too fast in the dendrites

However the polarity of the extracellular works out pretty well as we want it.
i.e. periph neg ≈ −2.0 mV
central pos ≈ +2.0 mV

set up 8208 with RACT = 10.
quenchs = 2.
ROUTs = 2.
and add $\varepsilon = 2$. to most peripheral dendritic
pt. also.

Next on p. 72

Stefanis thinks that normally, many cells do not invade antidromically & that invasion can be induced by depolarization, either by a drug, or by penetration with an intracellular electrode.

However, Gaba + Glutamate presumably provoked of inhibition, locking soma & producing a bigger gradient from soma to dendrites, esp when the dendrites fire, this gives larger current and larger ⊕ peak. If the final ⊖ is very large, this could mean soma fires late, (presumably skipped before where initial neg. was caused by hittoc)

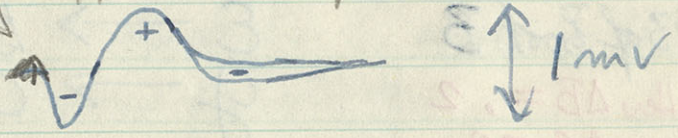
9/3/64

Talked with Stefanis (St. Elizabeths)
& Gordon

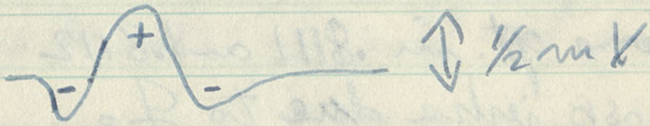
He records extracellularly from Betz cells, with + without drugs. He also has good intracellular records.

for antidromic, there is a small + due to approaching impulse

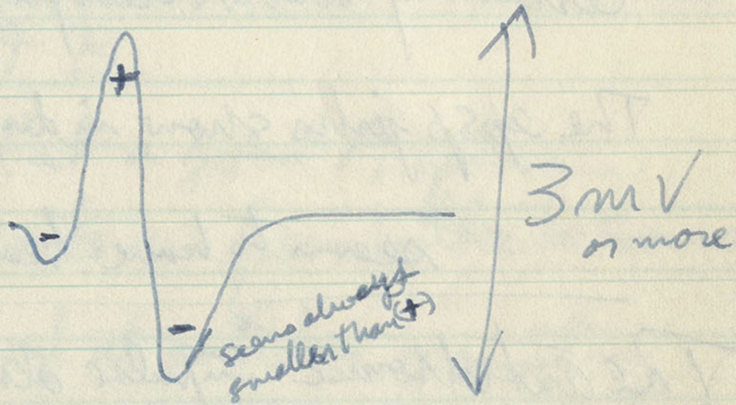
normal extracellular



glutamate increases rate of spontaneous firing.
(he says it depol. the cell)
depresses amplitude of extracell.



Gaba alone stops cell
but Gaba + glutamate
gives extra large
extracellular



My tentative interpretation: initial negativity came by soma firing. & axhilloc
(as in 1962 Biophys J.)

middle pos, if small, could be due to repol. of soma.
if large, presumed also due to dendritic firing.
& then last neg. due to dendritic repol.

~~largest record~~ glutamate depol. perhaps whole cell, but esp. dendrites.
and this favors dendritic firing & hence enhances
the middle ⊕ and final ⊖

9/4/64 Results.

The inhibitory J was too strong (also the E)

(probably due to AB & AC being in different units from E & J

see p. 93 of Book B

Here ΔB = .2
ΔC = 2.

E ⟶ B*RACT = Here 400.*B
J ⟶ C*QENCHA = 20.*C

Soma cpt. in .8111 and .8112 clearly shows ~~The~~ severe ipsp jerks due to J.

Certainly was successful in preventing soma firing.

The epsp jerks show in dendritic periphery for KT=5 and KT=15
seems to have been refractory at KT=10 and KT=20

The antidromic impulse almost succeeded, but inhibition was too severe.

reduce ΔB to 0.1
ΔC to 0.5 } for .8114–8116

9/3/64

Setup 64794.8111, .8112, .8113

which carry on from 64793.8104 & 8105
<u>cool kinetics</u>

with a new emphasis

The hope is that I.C. & dendritic E alone (.8113) will cause spontaneous firing.

That this plus soma trunk J will not (.8112)

& that ~~both~~, plus antidromic, will fire first in the dendrites and then in the soma, thus giving a somatic AB.

$\frac{USA}{UA} = \frac{10.}{25.}$ aimed at a good A spike
electrotonus from hillock to soma

$\frac{USD}{USA} = \frac{100.}{10.}$ aimed at milder geometry

Four NEJ aimed at sustaining the E & J for a longer time.

May wish to spot check this for one case.

$\boxed{\text{See p. 82}}$

Gordon likes $\frac{USD}{USA} = 40$. intuitively, in preference to 80.

perhaps should use 33.

setup 64791.~~[illegible]~~9601 as new variant of 0666 UA = 25.

with NJD = 5 and DZ = 0.1 ; UD = 100

if soma capacity is 2.5 times that of axonal cpt., get USA = 10.

and USD = 400.

implying that soma capacity is half that of combined dendritic first compartments.

9/4/64

Looking back at 64791.0666
.0669

To weigh suitability for paper, or how could be improved! Zero hour approaches, for writing the paper with Gordon.

In these two, we had CORE = .02 and $\frac{USD}{USA} = 80$.
also dendritic $Z = 0.625$ in .0666
$Z = 1.25$ in .0669

Probably too long.
Our latest review of Mitral Cells suggests the range 0.5 to 1.0 or 0.4 to 0.8 as closer

---

Soma

Also, here Threshold was close to 0.1
Whereas in current 64794.8800 series it seems to be around 0.25
* Could check & characterize by Threshold synaptic pot.
* Could do series to test Threshold at soma and dendrites.

In both 666 and 669 axon-soma delay was probably too large. (not sure really, except that there was reflected spk. in 669

*

Reconsider CORE and $\frac{USD}{USA}$ ratios

suppose $\frac{DD}{DA} = 3$, then $\frac{USD}{USA} = 5 \times (3)^2 = 45 \approx 40$

or suppose $\frac{DD}{DA} = 4$ for primary,
and 2.5 for four secondaries get $16 + 4(6.25) = 41$

Whereas CORE depends upon $\Sigma d^{3/2}$ and get $\approx (8+4+4)^{-1} \approx \frac{1}{24} \approx .04$

9/11/64

Try to catch up.
Have gotten snowed under this week, between doing many calculations & talking with Gordon about the write up, figures, terminology, etc.

Current Calculations are in ~~three~~ 5 series

~~Series~~ 64794.8800 antidromic, hot kinetics, active & passive varied USD and NJD and I.C.

Series 64794.8100 antidromic cooler kinetics → the later Stefani's problem
p.82

Series 64794.8200 granule cell problem (at first, just dendritic S.P. with secondary load

Series 64791.9600 modification of 64791.0666 Passive
64791 9900 " " 64791.0669 Active

9/11/64 64794.8200 Series

Granule cell extracellular Potential Model

Began p. 67 where have 64794.8206 & .8207

64794.8208 Here RACT = 10. ; ROUT & QENCH = 2.
use B = 2 in most periph cpt. also.
Interesting but cpts 1, 2, 3 & 4 fired in 2nd phase
(not wanted)
also cpt. 12 action pot. as large as 9 & 10

∴ Decided to increase B in cpt. 8
decrease B in cpts 10, 11, 12
& put long sustained C into 1, 2, 3 …

64794.8209 suppression of spike in 1, 2, 3 & 4
worked.
But got spike later as in 10, 11 & 12
Also peripheral sink relatively too strong
$V_e = 1.8$ at later peak $V_e = -1.6$ at peak

∴ Added stronger inhib. to cp. 7 & 10, 11, 12.

64794.8210 Worked quite well with regard to synchrony
of deep + & superficial − extracell.
However, neg was too large rel to pos.
∴ ~~increase~~ added C to cpt. 8 to
weaken sink & shift crossover

64794.8211 This worked rather well. Note the potential scale
is arbitrary. Here
Also τ is a free parameter need factor of 3 in plots

9/11/64

64794.8211 of previous page worked quite well for the granule cell problem.

deep pos $V_e \approx 3 \times (.94) \approx 3$ mV

~~deep~~ superficial neg $\approx 3 \times (-.73) \approx -2$ mV

with timing pretty well synchronous

However, decided that there is probably an earlier phase of granule cell soma & trunk inhibition which overlaps & distorts mitral cell transient. Therefore, set-up next problem with this in mind.

64794.8212 Not bad as a first try, but decide to have some E in dendritic periphery and also to strengthen E in cp. 8 rel to 12

also, try to minimize arbitrariness.

64794.8213 goofed by reversing $\overset{BEB}{B}$ & BJC cards for KEJ = 3

← rerun with this corrected & with minor changes.

64794.8214 (9/12/64) pretty fair but it looks as though

5 & 6 should be more inhib. for KT = 18-31

8-12 " " " excit. for KT = 14-17

also, overall sink could be slightly weakened.

∴ add an KEJ at KT = 12, add flattened J & make E fit better

9/11/64 64794.8800 Series continued from p. 66 + 65 74

64794.8821 Production Run (9/4/64) N58 = 8

IFVE = 1, IFAB = +1 UD = 200. Z = ~~.56~~ .57

corresp to ΔZ = .07

Hot kinetics, passive dendrites
no synaptic E

Perfectly good results, but meant to have UD = 100.

64794.8822 corresponding run for ~~[illegible]~~ active dendrites

Dendritic spike was essentially synchronous

apparent intracell conduct. vel. recip of x .01 τ for .56 λ

approx 400μ for .04 msec

approx 10 m/sec

Sign of reflected antidromic

Looking at extracellular dendritic pot.

it is possible, but not really legitimate, to coax out a 1.2 m/sec figure by taking (−+) crossover for ~~some~~ cpts 4−8 and neg peak for 11 & 12

However, near synchrony yields small amplitude extracellular pots.

grand extracellulars are good.

9/11/64 ✓ 75

64794.8823 $\boxed{\text{VD reduced to 100.}}$ $\frac{USP}{USA} = \frac{400.}{100.} = 40$

NJD = 5 IFVE = 0, IFAB = 0

I.C. = 0.2 in dendrites + soma
except cpt. 9

Active Case gave synchronous dendritic spike
Passive Case blocked at Soma

This shows again that cannot have simple pair.

64794.8824 similar, with NJD = 10

Active Case had very little axon-soma delay
& very little dendritic
increasing latency

Passive Case blocked at soma.

64794.8825 same as .8823 with IFVE = 1, IFAB = -1
except cpt. 9 also has I.C. = .2

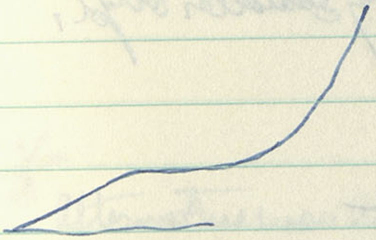
It is amazing to note how the 0.2 in cpt. 9
facilitated axon-dendritic invasion over 8823
In 8823, the soma fired at KT = 17
In 8825, the " " " " 14
and the dendritic spike is almost precisely synchronous

Consequently, Ve peak at soma is only .0186 ~~[illegible]~~ mV
negligible amplitude ~~[illegible]~~ V

9/11/64

64794.8826 same as 8825 except that I.C. = 0.3 in dendrites
IFVE = 0, IFAB = 0

active soma & dendrites fired ahead of 2&3
clearly dendritic I.C. above threshold.
for dendritic spike



Passive case was barely threshold for soma.
Took off after some delay

Again proves difficulty of simple active-passive pair.
Won't work with same I.C.

64794.8827 here NJD = 10 IFVE = 1, IFAB = -1
I.C. = 0.15 in soma & dendrites
Dendritic spike very nearly synchronous
Small extracellular
neg peak at soma = -0.34 mV
Equipotential Contours not too far off,
but amplitudes are small.

64794.8828 same as 8827 (NJD = 10)
but with IFVE = 0, IFAB = 0
I.C. = 0.3 in dendrites only

Active case, cpts 9-14 fired before #2-8

Passive case, barely threshold for soma.

64794.8831 showed that RBSQ = 0.5 had a slight effect compared with 8825, but not serious.

~~Dendritic spike now has~~ all spikes now have slightly smaller ampl.

.8832 blocked at soma

Decided to set up

.8833 with B = .05, .04, .03, .02, .01

for each KEJ

and .8834 .1, .08, .06, .04, .02

(9/12/64) opposite page

9/11/64

setup 64794.88~~25~~31 & .8832

.8831 to test effect of reducing RBSQ from 1.0 to 0.5

.8832 to test idea of getting decremental conduction in the dendrites by slugging C into the dendrites, graded ~~toward~~ periphery & also reducing ROUTC from 10. to 5.

* Alternative would be to modify program to permit UD to be nonsymmetric

This is related to notion that buildup of J is what causes soma to fail when loaded with passive dendrites & that this has resemblance with accomodation & can give grades of decremental conduction.

Maybe Dick FitzHugh's concern about the possibility of a second stable state can be turned to profit here. Perhaps this is an accomodative state whose stability need not be absolute because we could bring in a slower recovery process.

population of mitral cells during antidromic invasion. The other consists of a different sequence of membrane potential gradients in ~~individual~~ ~~[illegible]~~ cells of the granule cell population. Mitral-GEC and Granule-GEC.

9/4/64 Yesterday Gordon & I discussed write up

Need to distinguish clearly between the apparent phases of an observed extracellular potential transient and the hypothetical underlying generators of the extracellular current which produce these potentials.

Underlying inhomogeneity or non-uniformity or gradient in the membrane of a single cell is needed to generate extracellular current. Can be a non-uniform conductance change, or simply a non-uniformity of residual membrane' potential

Possible Names

ULCGI underlying current generating inhomogeneity

* GEC (Generator of Extracellular Current) (in general, can include electrodes)

NGEC Neuronal Generator of Extracellular Current

NMGGEC Neuronal Membrane Gradient which Generates Extracellular Current

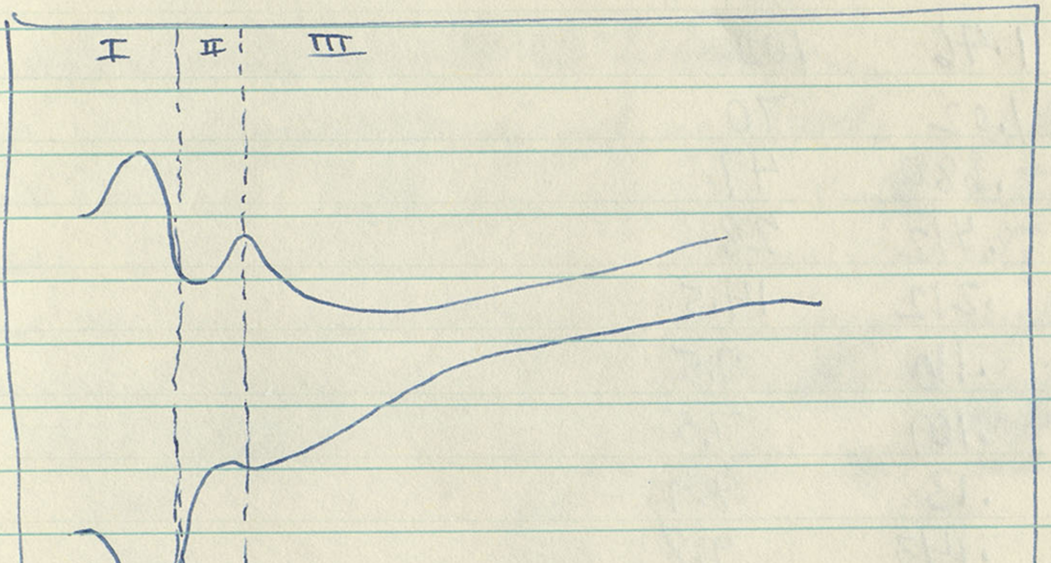
But perhaps GEC is best, with lot of elaboration.

Model assumes that 1st approx can be achieved by means of two **GEC**. One of these consists of the sequence of membrane potential gradients in each cell of the

9/11/64

The paper will need a table of Definitions, including such items as

GEC
Mitral-GEC
Granule-GEC
$\mathcal{E}$
g
CORE
USD/USA ≡ Geometric Hurdle
Z-length
Shunt Factor (External Potential Divider)
Response Periods I, II, III
Kinetic Constants
Increase of Latency with Distance.



slight shift of I-II boundary probably due to ~~spread~~ overlap from Granule GEC

Attenuation of neg. peak is a crutch. Should not present, better to present Ve vs depth at several different ~~Times~~

	peak neg	percent
	64794.8821	
		%
4	1.46	100
5	1.02	70
6	.680	47
7	.412	28
8	.212	14.5
9	.110	7.5
10	.109	7.5
11	.13	8.9
12	.143	9.8

0.56λ

9/11/64

Some quantitative checks, also plot of attenuation

in 64791.0669 (active) at soma level $\left|\frac{\text{pos peak}}{\text{neg peak}}\right| = \frac{1.13}{1.59} = 0.71$

at glomerular level $\left|\frac{\text{peak neg}}{\text{peak pos}}\right| = \frac{.285}{.385} = 0.74$

which verifies that theoretical surface record is inversion of deep record

∴ peak to peak amplitude: $\left|\frac{\text{soma}}{\text{glom}}\right| = \frac{2.72}{0.67} = 4.06$

which comes directly from potential divider assumption of the model

---

in 64791.0666 (passive) at soma level $\left|\frac{\text{pos peak}}{\text{neg peak}}\right| = \frac{.451}{1.43} = 0.315$

at glomerular $\left|\frac{\text{neg}}{\text{pos}}\right| = \frac{.115}{.345} = 0.334$

The data consulted seems to lie in between.

Also, when ~~decrement of~~ neg peak amplitude is plotted vs distance find that exp. falls more sharply than active dendrite case, but more slowly than passive dendrite case.

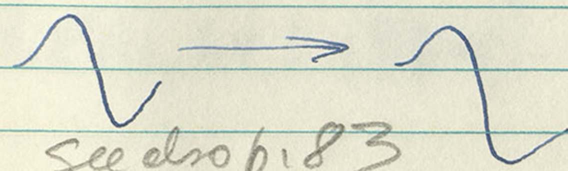
Also, ~~exp.~~ case does not seem to give a min. amplitude as record turns over? This fits ~~better~~ ? the short passive case.
shorter

	.0669 % of max neg peak		.0666 % of max neg peak passive		approx data
cpts 4	100		100		100
5	99		55		75
6	92		26		65
7	74		10.5		53
8	37		6.8		
9	18	1.25λ	8	.625λ	40

or maybe neg. everywhere
due to current flow to the
terminal sinks of afferent
fiber terminals, which would
be most neg. deep and less
neg toward surface (an external shunting current)

9/11/64 (9/10/64)

Although the computed surface record is a perfect inversion, with rescaling, of the deep record, This is not true of the experimental record. The experimental surface record tends to favor the neg. peak (II) over the pos (I)



& the crossover & peaks seem a little earlier.

see also p. 83

This might all be explained by an overall neg. drift which might be an early effect of the granule-GEC

This idea requires that granule cells receive some early inhib. input at the same time as the mitral cell soma repolarizes. Gordon says that this is possible ~~in terms~~ by means of other fibers in the stimulated tract; these are large and would conduct fast enough; he wants to recheck that anatomical & physiological evidence.

Furthermore, if this stands up, it could account for less shift of the mitral soma level extracellular record, because there we are near zero contour (mit. pt.) of the granule cell field. Input could even start on the neg side of zero contour. This could probably account for the imperfect "phase" ~~not exactly~~ relation ~~of~~ between the surface & mitral cell level records. This complication need not be discussed at beginning of paper. There might focus on the inversion aspect of these records

9/12/64 Brief review of the 64794.8100 series which attempts to to compare three cases ⓐ dendritic E alone to give spont. firing
ⓑ plus somatic J to suppress " "
ⓒ plus antidromic which helps dendrites to fire ahead of soma

64794.8111, 2&3 (9/4/64) J was too strong at soma, but did not prevent periph dendritic spike,
some E pulses reveal refract or accomodated state

64794.8114, 5&6 (9/5/64) here J was too weak.
also some cards reversed.

64794.8117, 8&9 (9/8/64) goofed with E = .075
format picked up 50.
(9/9/64) rerun with E = 0.07
~~64794.8121~~ needs stronger J

64794.8121, 2&3 (9/10/64) getting better, but need to delay antidromic spike
& avoid KT=12 J

64794.8124, 5&6 (9/10/64) Here delayed spike by adding J to axon.
Soma not invaded antidromically,
otherwise pretty close.

64794.8127, 8&9 reduce quench & ROUTE use NSP
(9/11/64) & simplify I.C.

64794.8131, 2&3
(9/12/64) ? machine error? goofed in setting VSP = 5. instead of 0.5
further reduce ROUTE

9/14/64 83

Some surface records eg Prod 3 & Prod 2 of April 12
also May 16

Surface pos. lines up well with the deep negativity. surface neg not so obvious

But in May 2 (illustration series)

May 31 Prods 1 & 2
surface records small
~~& surface pos leads the deep neg.~~
presumably $\simeq \frac{1}{20}$ pot. divider effect.

probably more surface saline

March 29 surface + leads ~~deep~~ neg slightly

Surface neg. might be due to afferent axon GEC

9/15/64

64794.8833 & 4 attempt at decrementally conducted dendritic spike J not enough I.C. plus E was too much

Actually, the dendritic spike occurred before the hilloc spike. Could rerun with dendritic I.C. reduced to zero.

64794.8215 granule cell approx worked pretty well

Could smooth the E somewhat at KEJ = 3 & 4.

Maybe eliminate E from KEJ = 1

64794.8131, 2 & 3 Dendritic E, J & antidromic series axonal spike failed because of axonal J also initiated too late

The E alone is OK and will not need to be repeated i.e. 64794.8133 very similar to 64794.8129 rel. IR drop along cone of extracellular volume associated with each mitral cell.

	IR drop rel. to surface For a const. radial current.	Rescaled increments
surface	0	.199
gpt. 9	0.2	.066
8	0.265	.072
7	0.337	.080
6	0.417	.090
5	0.507	.101
mitral soma I	0.608	.114
•	0.722	.130
	0.852	.149
1mm. deep	1.000	
		1.001

But now the question is: For current generated outside the conical element, how much IR drop is there from IND electrode to the bulb surface? How

9/15/64 - 9/16/64

Consider the radial aspect of Re in Olfactory Bulb.

Estimate Radii of curvature at different levels

bulb surface ~2.0 mm
glomerular level 1.7
mitral cell 1.3
deep granular 1.0

$$\frac{dR}{d\rho} = \frac{Re}{4\pi\rho^2}$$

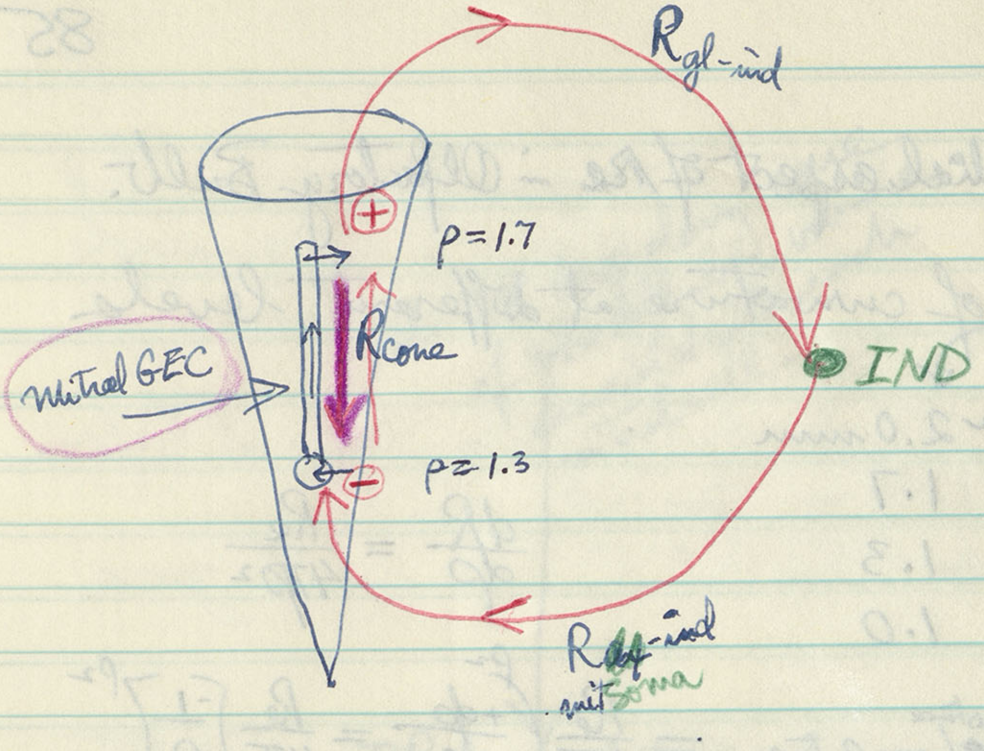
let ρ represent radius, then ~~R~~ resistance from ρ_1 to ρ_2 $= \frac{Re}{4\pi}\int_{\rho_1}^{\rho_2} \frac{+d\rho}{\rho^2} = \frac{Re}{4\pi}\left[\frac{-1}{\rho}\right]_{\rho_1}^{\rho_2}$

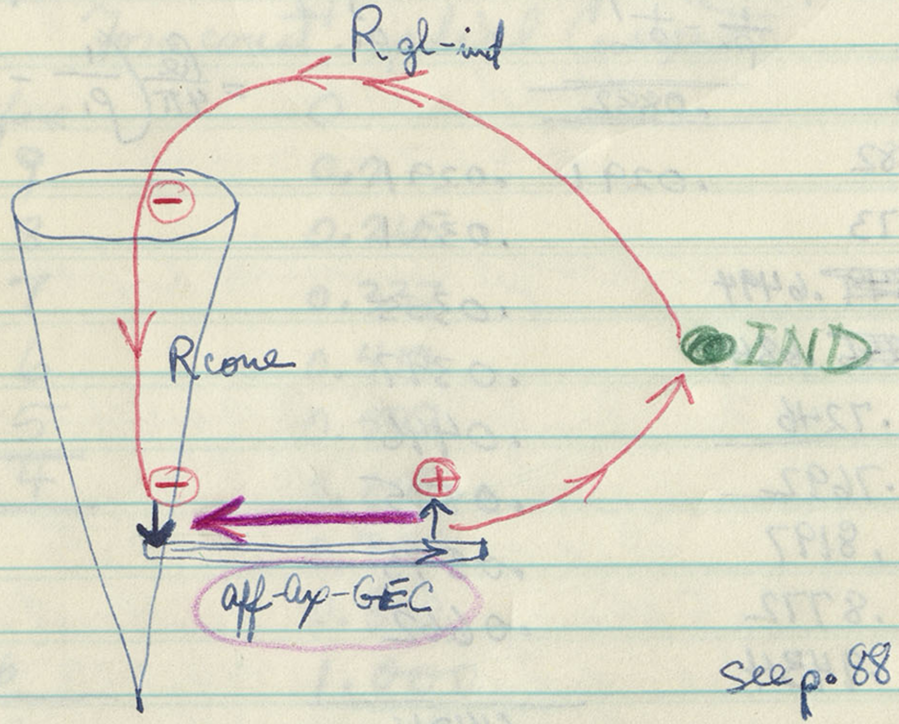
$$= \frac{Re}{4\pi}\left(\frac{1}{\rho_1} - \frac{1}{\rho_2}\right)$$

		ρ	$\frac{1}{\rho}$	$\frac{1}{\rho_1} - \frac{1}{\rho_2}$	
surface		2.0	.50	.0882	
epl	9	1.7	.5882	.0291	.0291
	8	1.62	.6173		.0321
	7	1.54	~~.6849~~ .6494		.0355
	6	1.46	~~.7246~~ .6849		.0397
	5	1.38	.7246		.0446
soma	4	1.30	.7692		.0505
axonal	3	1.22	.8197		.0575
	2	1.14	.8772		.0662
	1	1.06	.9434		
					.4434

rescale

does this compare with the drop along the cone.


R gl-ind
⊕
p=1.7
Rcone
mitral GEC
⊖
p=1.3
IND
R ~~off~~-ind
mit soma


R gl-ind
⊖
Rcone
IND
⊖
⊕
aff-ax-GEC

See p. 88

9/16/64

Consider the possibility that $R_{cone} = \left(R_{\text{gl-ind}} + R_{\text{ax-ind}}\right)$

Then the -2 mV difference between the deep and the surface record means that open circuiting the external path would ~~increase the~~ make the deep record equal -4 mV (now isolated from outside)

Since we estimate that $\frac{R_{\text{gl-ind}}}{R_{\text{ax-ind}}} \simeq \frac{1}{4}$

We would have
$$R_{\text{gl-ind}} = 0.2\ R_{cone}$$
$$R_{\underset{soma}{ax}\text{-ind}} = 0.8\ R_{cone}$$

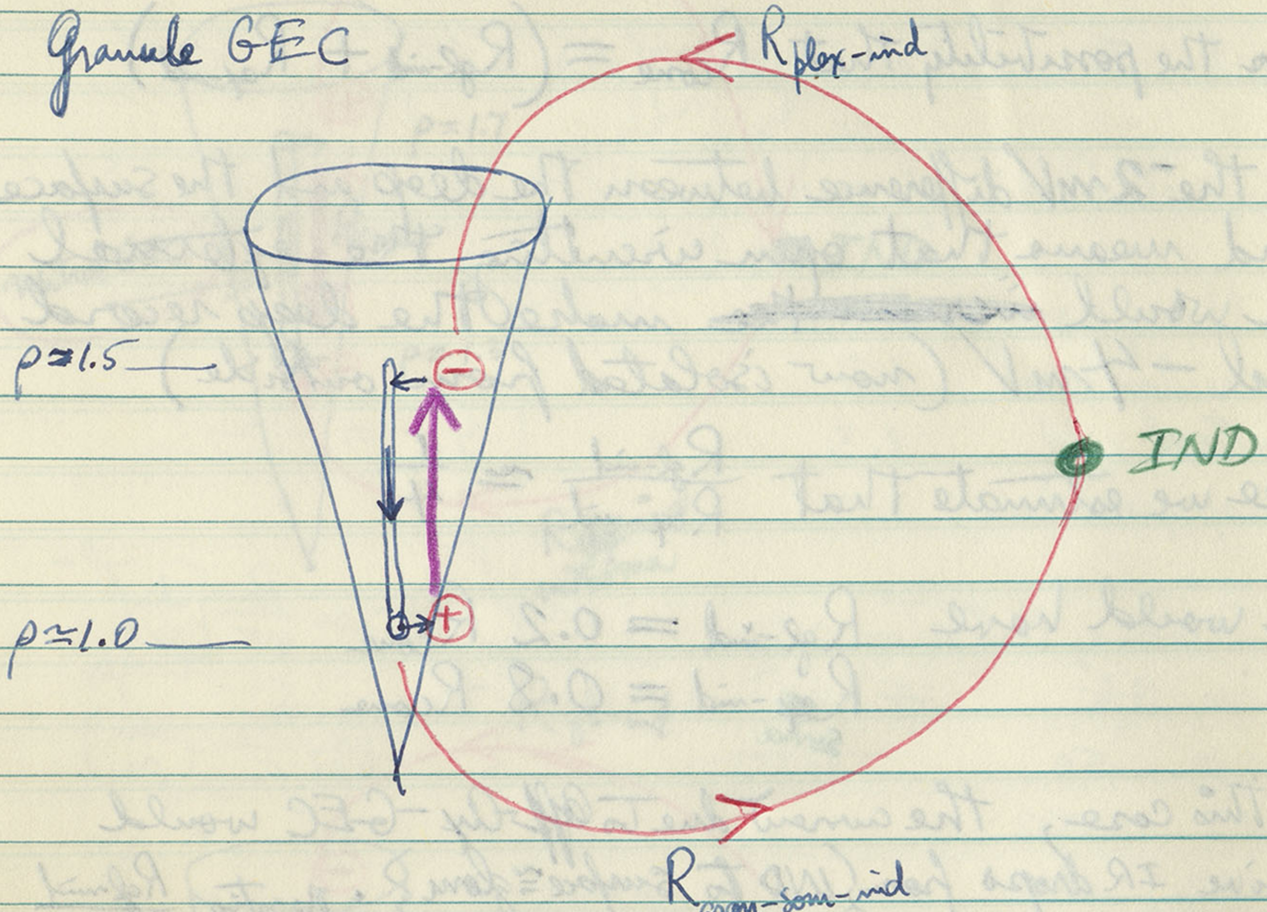
In this case, the current due to Off-Ax-GEC would give IR drops from $\left\{\frac{\text{IND to surface} \cong \text{glom}}{\text{surface} \cong \text{glom to deep}}\right\}$ in the ratio $\frac{R_{\text{gl-ind}}}{R_{cone}} = 1/5$

$$\frac{\text{surface ampl}}{\text{deep ampl}} = \frac{1}{6}$$

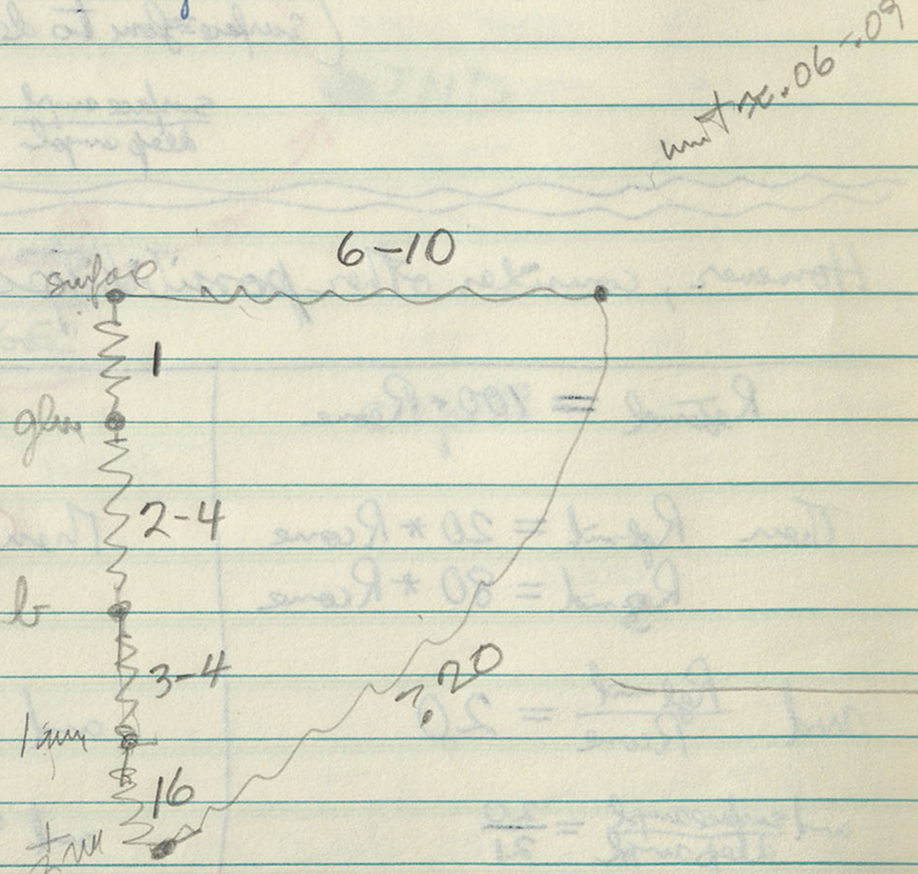
However, consider other possibilities

$R_{external} = 100 * R_{cone}$	$R_{external} = 5 * R_{cone}$
Then $R_{\text{gl-ind}} = 20 * R_{cone}$ $R_{\underset{S}{ax}\text{-ind}} = 80 * R_{cone}$	Then $\boxed{R_{\text{gl-ind}} = R_{cone}}$ see next page $R_{\underset{S}{ax}\text{-ind}} = 4 * R_{cone}$
and $\frac{R_{\text{gl-ind}}}{R_{cone}} = 20$	and $\frac{R_{\text{gl-ind}}}{R_{cone}} = 1$
and $\frac{\text{surface ampl}}{\text{deep ampl}} = \frac{20}{21}$ for Off-Ax-GEC	and $\frac{\text{surface ampl}}{\text{deep ampl}} = \frac{1}{2}$

Granule GEC



$R_{glom\text{-}ind}$
$R_{plex\text{-}ind}$
$R_{mb\text{-}ind}$
$R_{gsb\text{-}ind}$



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Compare conical resistance from $\rho = \frac{1}{2}$ mm to $\rho = 1$ mm $\qquad \frac{1}{1/2} - \frac{1}{1} = 1$

$\rho = 1$ mm to $\rho = 2$ mm $\qquad 1 - \frac{1}{2} = \frac{1}{2}$

$\rho = 2$ mm to $\rho = \infty$ $\qquad \frac{1}{2} - 0 = \frac{1}{2}$

However R_{cone} is from mitral soma level to glomerular level

$\rho \approx 1.2$ to 1.3 $\qquad \rho = 1.7$ to 1.8

$$\therefore \text{ this resistance } \propto \begin{cases} \frac{1}{1.2} - \frac{1}{1.8} = .833 - .556 = .277 \\ \frac{1}{1.3} - \frac{1}{1.7} = .769 - .588 = .181 \end{cases}$$

say 0.2 to 0.25

$$\text{Resistance from glom to surface } \propto \begin{cases} \frac{1}{1.7} - \frac{1}{2} = .588 - .5 = .088 \\ \frac{1}{1.8} - \frac{1}{2} = .556 - .5 = .056 \end{cases}$$

Resistance from surface to ∞ $\quad \propto \frac{1}{2} - 0 = 0.5$

surface to $\rho = 4$ $\quad \propto \frac{1}{2} - \frac{1}{4} = 0.25$

Resistance from $\rho = 1$ to $\rho = 1.3$ $\quad \propto 1. - .769 = 0.231$

$\rightarrow \rho = \frac{1}{2}$ to $\rho = 1.3$ $\quad \propto 2. - .769 = 1.231$ 1.2

How much of this applies can be estimated from deep gradients caused by the external loop current, which would be 1/6 of the GEC current for the case $R_{ext} = 5 \times R_{cone}$

$\rightarrow R_{gl-mod} \approx 10$

$R_{m-mod} \approx 40$

$$\therefore \frac{R_{ext}}{R_{cone}} \approx \begin{cases} \frac{50}{2.5} = 20 \\ \frac{40}{4} \approx 10 \end{cases}$$

9/16/64

Afferent Axon GEC would generate same current as mitral axon spike if $\Sigma d^{3/2}$ were the same.

Mitral cell axon spike ~~≈~~ $\frac{1}{25}$ current of mitral soma spike because CORE estimated as 0.04

See p. 70

assuming similar spike duration & kinetics

Cajal says these afferent axons are sparse in the tract, but they bifurcate several times and then form a very extensive arborization (plexus) in granule cell layer.

Suppose the plexus $\Sigma d^{3/2}$ were as much as ten time that of mitral axons. Then we would expect $(10)(.04) = 0.4$ of mitral soma current, & thus about 0.8 mV neg peak deep

and from bottom corner of p. 86, surface neg might be 0.4 mV

Note: to get anything at surface, require that $\frac{R_{surf-mid}}{R_{core}} > 0$ not negligible

Need to modify program.

KVE = 1 computes V_e for no shunt

KVE = 2 " " for ϵ shunt current (potential divider effect)

Need to shift from ①-⑨ to JS-JNZ

KVE = 3

Could combine Ⓐ with KVE = 2

Ⓐ effect of significant currents including axonal cpts

Ⓑ effect of conical r_e including axonal compartments

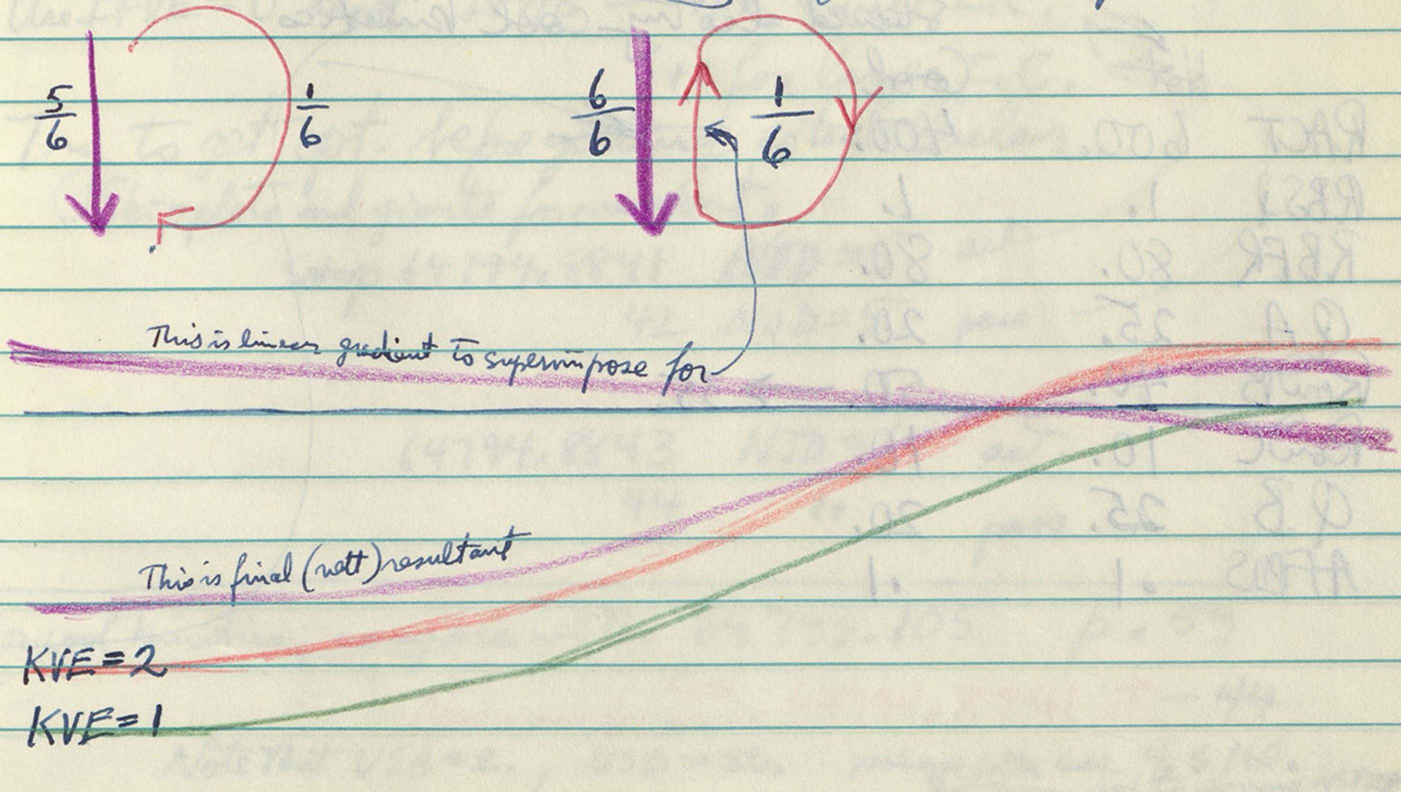
9/16/64

Refer back to p. 29 of Book 3

Mitral soma Vi is a voltage source which puts out a current determined by Z_N which depends mainly upon R_m, R_i and geometry. Presumably not much affected by Re. If this is so, small changes in external conductance would not change ~~the total~~ amount of external current.

Thus mitral GEC is a current generator.

If the external loop path has a conductance which is not negligibly small, it must divert some of the GEC current & reduce the "apparent ext. driving potential". This is equivalent to imposing a steady current along Re, which would cause a linearly graded drop.



If 41-44 series give trouble consider using IFTEST to determine whether BEB & BJC are needed.

St. St. with I.C.

might save computation time by making USA = 5. USD = 200.

instead of 10. 400.

These are hot kinetics. Should also try cool kinetics

	Hot	Cool
RACT	600.	400.
RBSP	1.	1.
RBER	80.	80.
QA	25.	20.
RowB	40.	50. → 35.
RowC	10.	10.
QB	25.	20.
AFPOS	.1	.1

9/17/64 Setup new computations.
compare with p. 84

64794.8835 & 6 The I.C. were removed from 33 & 34
also doubled J values

for 7 & 8

in 35 first BEB & BJC pair reversed & rerun
in 36 This was OK, but cpts 4 & 5 fired a little too soon & 8 perhaps too late.

Probably best to weaken E & perhaps make uniform.

looking back over 8831 — 8836, decide to try J of 36
together with I.C. = 0.1 in soma & dendritic cpts
(zero in one case)
and B = 0.05 in " — — — —,
except 1.5 in 9th

for 64794.8837 & 38
Increase to 10 compartments & try again for decremental cond.

Compare with p. ~~76~~ 75 & 76 64794.8826, 27 & 28
23, 24, 25

Use IFVE = 0 and IFAB = −1 for small I.C.,
+1 for larger I.C.

Try to get opt. before getting extracellular.
Skip plots and giants for moment.

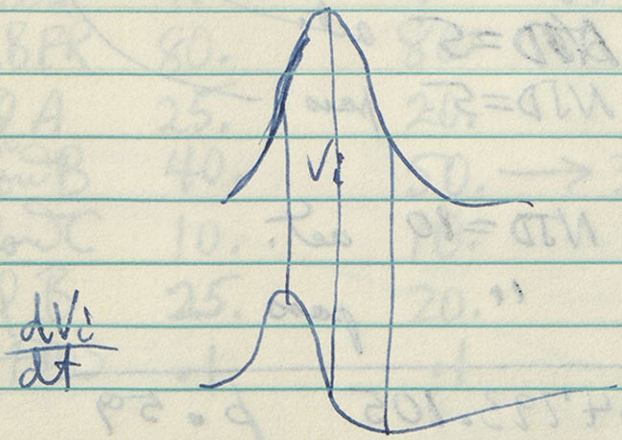
Setup 64794.8841 NJD = 5 act.
42 NJD = 5. pass

64794.8843 NJD = 10 act.
44 " pass

For cool kinetics, compare with 64793.105 p. 59

New name for cool series 64794.8741 etc — 44

Note that USA = 2., USD = 80. perhaps better use 4. & 160.
But then need to increase NSTEP



This limiting case reduces amplitude →

9/17/64

Consider active versus passive

$\boxed{A}$ In period I, the deep neg. and the surface pos. are provided equally well by the active and the passive, or a decremental case.

$\boxed{B}$ Period II is more diagnostic, but is unfortunately experimentally muddy, because of GEC overlap.

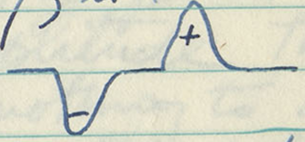
Consider only the **Mitral-GEC**

Consider first only the deep record versus surface without any external path shunting.

This is like recording from an axon in oil

---

① If dendritic spike propagates very slowly, it is like two electrodes far apart in oil.



The neg & pos. phases are exactly the same except for sign and displacement, provided that soma spike and peripheral dendritic spike are exactly the same & the delay is long enough that ~~each~~ when ~~one~~ electrode has spike, other electrode has rest. $V_m \overset{zero}{=} E_r$

② However, for very fast propagation and uniform spike shape, the record approaches the first time derivative, where the pos phase is smaller than the neg phase because # the intracellular spike declines more slowly than it rises

9/17/64

In both cases, pot. divider effect would make surface record a reduced inversion of the soma record.

✱ The point is that the $\frac{dV_i}{dt}$ effect for the prop. dendritic spike does give neg.(deep) larger than deep pos. Which reduces difference from passive case.

This was, in fact, shown by 64791.0669

✱ This optimal active case does not so much need cool kinetics as it needs somewhat slower falling phase.

However Gordon's records indicate that this ~~[illegible]~~ of Period II is moderately sharp, at least in the illustrative records, neg in mid region

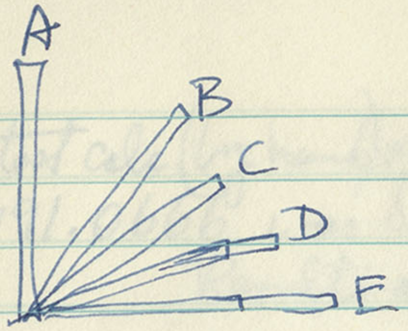
③ In the passive case, necessarily get period II disturbance to be of smaller amplitude than that in period I, but this has nothing to do with derivative of intracellular action potential. This is differencing of soma intracellular spike against the later, smaller electrotonic version found at dendritic periphery.

However, period II is complicated by granule & afferent GECs.

Also, period II is more subject to any smear due differences between primary & secondary dendrites.

see next page.

9/17/64



A = primary
B, C, D & E represent different sec. orientations

1st approx. Suppose intracellular events are the same in all of them. Actually, λ + length variation could cause some temporal dispersion.

B drives its current across 3/4 of cone resistance of A
C 1/2
D 1/4
E 0

∴ IR drops should be proportional to these i.e. IR drops rel. to surface.

Consider depth potentials rel. to unshunted glomerular level

cpt. levels	4	5	6	7	8	9
A primary	1×④	1*⑤	1*⑥	1*⑦	1*⑧	1*0
B secondary	$\frac{3}{4}$×④	$\frac{3}{4}$*(5-6)	$\frac{3}{4}$*(6-7)	$\frac{3}{4}$*⑧	0	0
C secondary	$\frac{1}{2}$*④	$\frac{1}{2}$*⑥	$\frac{1}{2}$*⑧	0	0	0
D "	$\frac{1}{4}$*④	$\frac{1}{4}$*⑧	___	___		
	2.5*④					

Dividing by 2.5, get weight factors A 0.4, B 0.3, C 0.2, D 0.1

9/17/64

A test calc. (by hand) of primary-secondary smearing. 64791.0666 was carried out.

Results attached.

Conclusion: That the crossover from surface type record to deep type record gets shifted deeper than for primary only.

In this case, the smeared ~~record~~ transient at cpt. ⑥ is in the transition crossover region, whereas the primary ~~record~~ transient at cpt ⑥ was of the deep type. For the primary dendrite transient, the transition crossover type transient occurred at cpt. ⑦. All of these, of course, include the potential divider effect

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Irving Gillespie

Photography
Mr. Godwin 62251
discussed photog. of
plotted projections of trees

p.57

try $V = .4$ $V^2 = .16$ $V^4 = .0256$

$R_1V^2 = 80$ $R_2V^4 = 1024$

Sum is 1104

$J_{ss} = \frac{1104}{200} = 5.52$

$\mathcal{E}_{ss} = \frac{1104}{55.52} = 19.9$

$\psi_{ss} = 0.4 - (19.9)(0.6) + \overset{2.76}{(\boxed{5.52})}(.5)$

$= 3.16 - 11.93 = -8.77$

---

try $V = .6$ $V^2 = .36$ $V^4 = .1300$

$R_1V^2 = 180$ $R_2V^4 = 5200$

Sum is 5380

$J_{ss} = \frac{5380}{200} = 26.9$

$\mathcal{E}_{ss} = \frac{5380}{76.9} = 70$

$\psi_{ss} = 0.6 - (70)(.4) + \overset{18.8}{26.9(.7)}$

$= 19.4 - 28 = -8.6$

try $V = .7$ $\quad V^2 = .49 \quad V^4 = .24$

$R_1V^2 = 245 \quad R_2V^4 = 9600$

Sum is 9845

$$J_{SS} = \frac{9845}{200} = 49.225$$

$$\mathcal{E}_{SS} = \frac{9845}{99.225} \triangleq 99.2$$

$$\Psi_{SS} = 0.7 - (99.2)(.3) + (\overset{39.4}{49.225})(.8)$$

$$= 41.1 - 29.7 = +11.4$$

This has crossed over

Root must be approx .64

$V^2 = .41 \quad V^4 = .168$

$R_1V^2 = 205 \quad R_2V^4 = 792$

Sum is 8125

$$J_{SS} = \frac{8125}{200} = 40.62$$

$$\mathcal{E}_{SS} = \frac{8125}{90.62} = 89.6$$

$$\Psi_{SS} = 0.64 - (89.6)(.36) + (\overset{(30.1)}{40.62})(.74)$$

$$= 30.74 - 32.3 = -1.56$$

Compare stability of J versus V plot

at

Ⓐ	Ⓒ
$\mathcal{E} = 0$	$\mathcal{E} \simeq 90$
$J = 0$	$J \approx 41$
$V = 0$	$V \approx .64$
$I = 0$	$I \approx -1.5$

What happens if we add ΔV to V by means of δ pulse.

In Ⓐ get $\tau \dot{V} = -\Delta V$, which is restorative.

In Ⓒ get $\tau \dot{V} \simeq -\Delta V(1 + \mathcal{E} + J)$

$\simeq -131(\Delta V)$ which is strongly restorative.

~~In Ⓐ get~~ $\tau \dot{J} = 0$ for instantaneous δ pulse of charge.

however $\tau \dot{\mathcal{E}} = R_1(V + \Delta V)^2 - R_1 V^2 + R_2(V + \Delta V)^4 - R_2 V$

$= R_1(2V\Delta V + (\Delta V)^2) + R_2(4V^3 \Delta V + \ldots$

See how instability of middle point shows up follows p ⑤ of yellow sheets

8/14/64

Now try $V = .09$

$V^2 = .81 \times 10^{-2}$ $V^4 = .656 \times 10^{-4}$

$R_1V^2 = 4.05$ $R_2V^4 = 2.62$

$\therefore R_1V^2 + R_2V^4 \simeq 6.67$

$J^{\cancel{8}}_{ss} = \frac{6.67}{200} = .0333$

$\mathcal{E}_{ss} = \frac{6.67}{50 + .033} = .133$

$\psi_{ss} = .09 - .133(.91) + \overset{.0063}{.0333(.19)}$

$= +.0963 - .1213$

$= -0.025$

This is closer to the middle point.

Next try $V = .08$ which will probably cross ψ to pos.

$V^2 = .64 \times 10^{-2}$ $V^4 = .41 \times 10^{-4}$

$R_1V^2 = 3.2$ $R_2V^4 = 1.64$

Sum $= 4.84$

$J_{ss} = \frac{4.84}{200} = .0242$ $\mathcal{E}_{ss} = \frac{4.84}{50 + .024} = .097$

$\psi_{ss} = .08 - \overset{.0892}{.097(.92)} + \overset{.00436}{.0242(.18)}$

$= +.084_4 - .0892$

$\simeq -.005$

which is very close

try $V = .075$ $V^2 = .563 \times 10^{-2}$ $V^4 = .317 \times 10^{-4}$

$R_1V^2 = 2.81$ $R_2V^4 = 1.264$

Sum $= 4.07$

$J_{ss} = .0203$ $\varepsilon_{ss} = .0814$

$$\psi_{ss} = .075 - (.0814)(.925) + \overset{.00355}{(.0203)(.175)}$$

$$= .07855 - .0753$$

$$= +.003$$

∴ Crossover is approx at $V = .077$

Now, try for third crossover

Begin with $V = .12$ $V^2 = 1.44 \times 10^{-2}$ $V^4 \approx 2.08 \times 10^{-4}$

$R_1V^2 = 7.2$ $R_2V^4 \approx 8.32$

together get 15.52

$J_{ss} = .0776$ $\varepsilon_{ss} = .3105$

$$\psi_{ss} = .12 - (.31)(.88) + \overset{.017}{.0776(.22)}$$

$= .137$ ~~[illegible]~~ $-$ ~~.352~~ $.273$

~~$\approx -.06$~~ ~~$\approx$~~ $-.136$

~~∴ neg minimum probably lies near 0.11~~

~~& we need to go farther~~

try $V = .14$

$V^2 = 1.96 \times 10^{-2}$ $V^4 = \overset{3}{3}.84 \times 10^{-4}$

$R_1 V^2 = 9.8$ $R_2 V^4 = 15.36$

$\text{Sum} = 25.16$

$J_{ss} = .125$ $\varepsilon_{ss} = \frac{25.16}{50.125} = .502$

$$\psi_{ss} = 0.14 - (.502)(.86) + \overset{.03}{(.125)(.24)}$$

$$= 0.17 - .43$$

$$= -.26$$

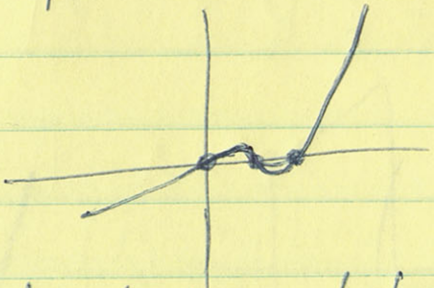
In other words, have farther to look for this.

guess around $V = .3$ or $.4$

When find it, need to investigate its stability.

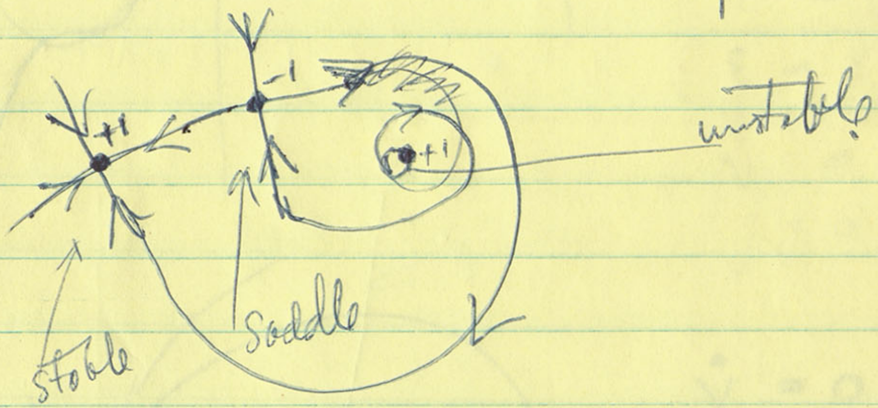
6/18/64 ①

Talked with Dick Fitzhugh
He had two suggestions
① Compute Ess & Jss for small V
& then ~~[illegible]~~ compute & plot I-V curve
~~two~~ see if there are Three singular points.

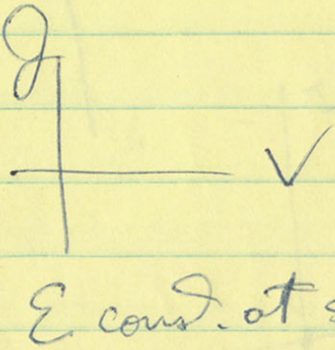


If so, investigate third to see if it is unstable.

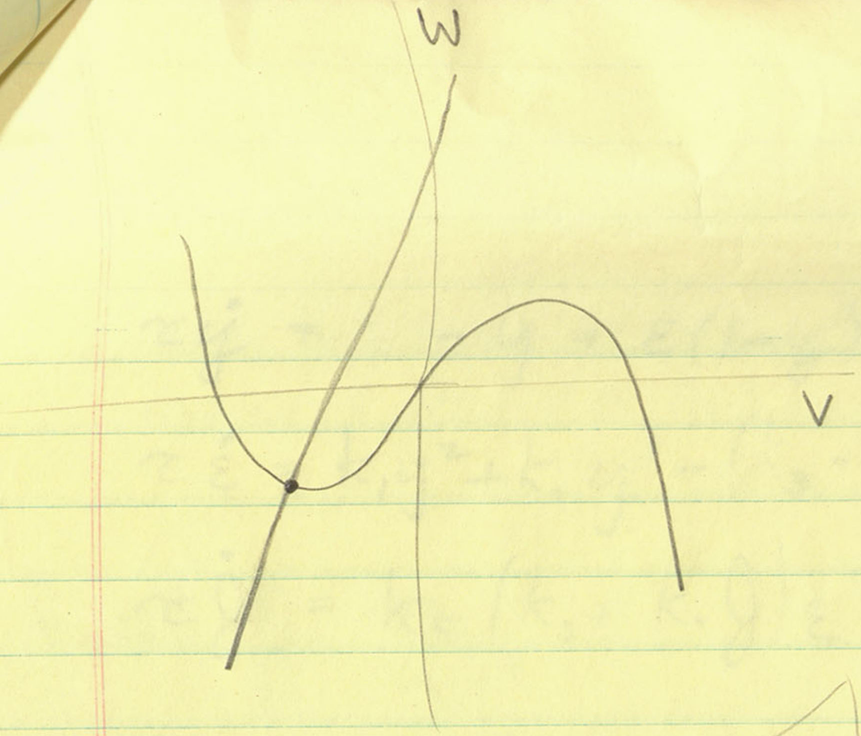
He says it could conceivably be, but he has not met this before

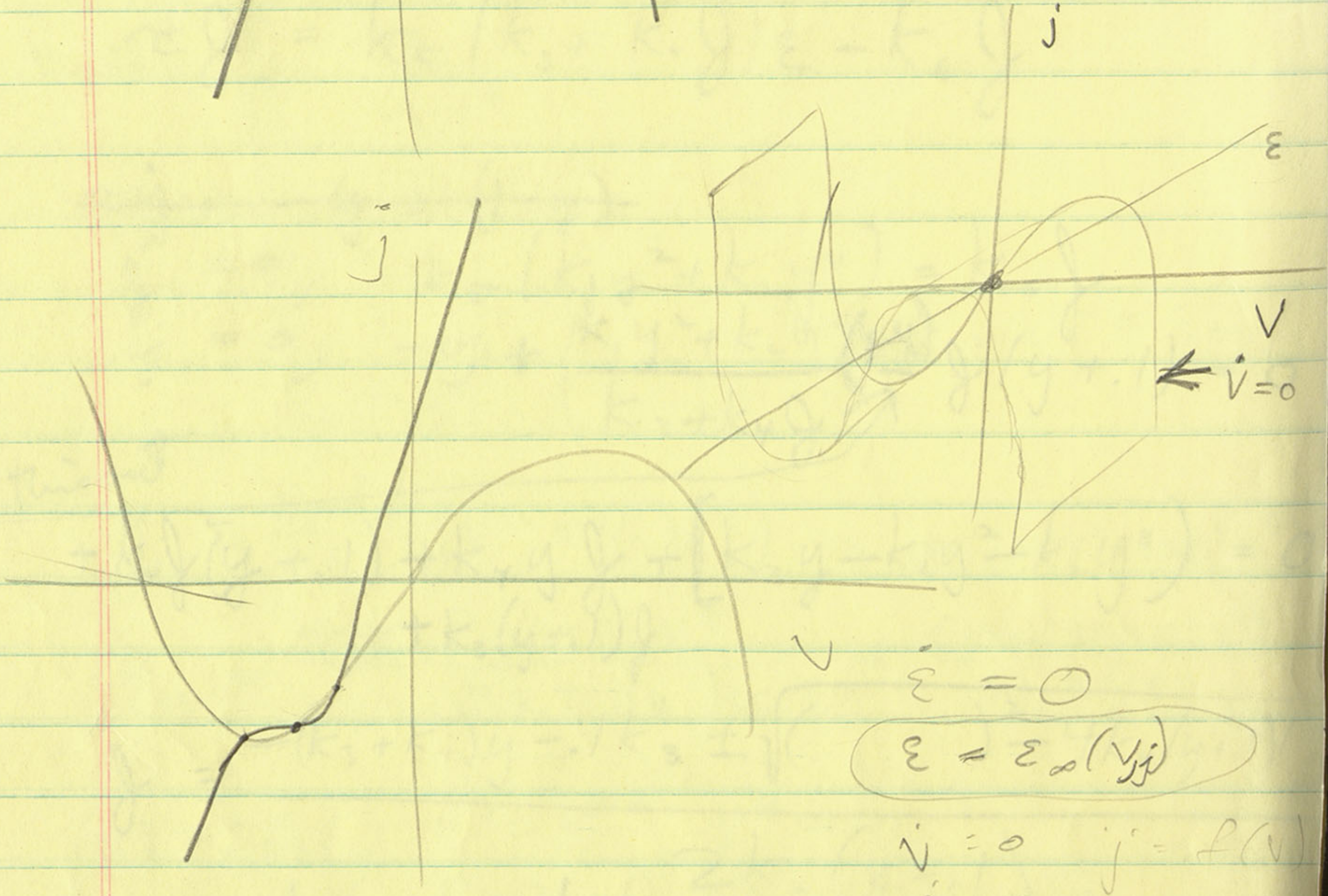


Also, plot



for E const. at st-st. value to corresp to BVP



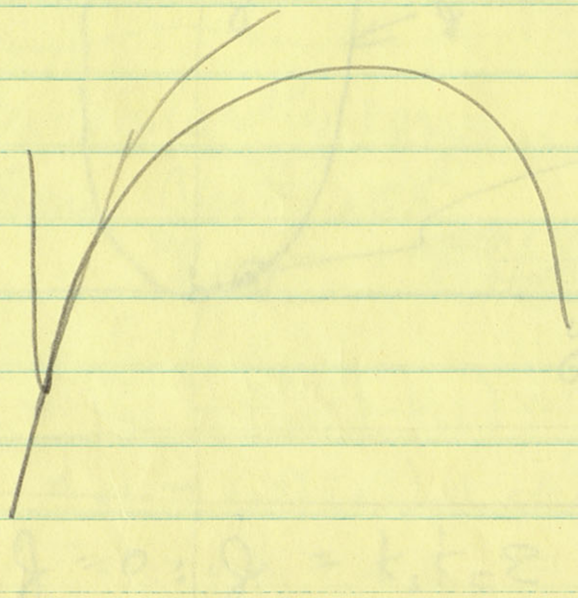


$$\dot{\varepsilon} = 0$$

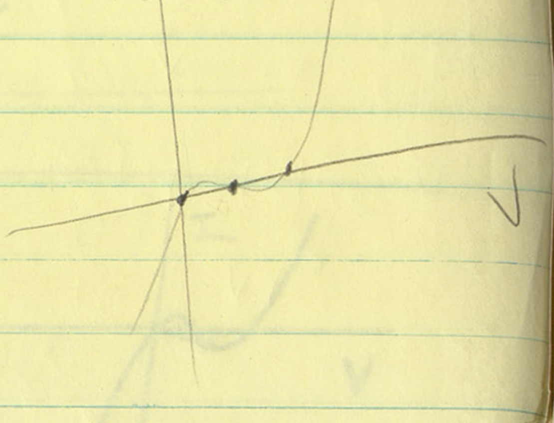
$$\boxed{\varepsilon = \varepsilon_\infty(V,j)}$$

$\dot{V} = 0 \quad j = f(V)$

$\dot{j} = 0$



$$\dot{V} = 0$$



$$\tau\dot{y} = -y + \varepsilon(1-y) - g(y+.1)$$

$$\tau\dot{\varepsilon} = k_1y^2 + k_2y^4 - (k_3+k_4g)\varepsilon = 0$$

$$\tau\dot{g} = k_5(k_3+k_4g)\varepsilon - k_6g$$

~~$\tau\dot{y} = -y + (1-y)$~~

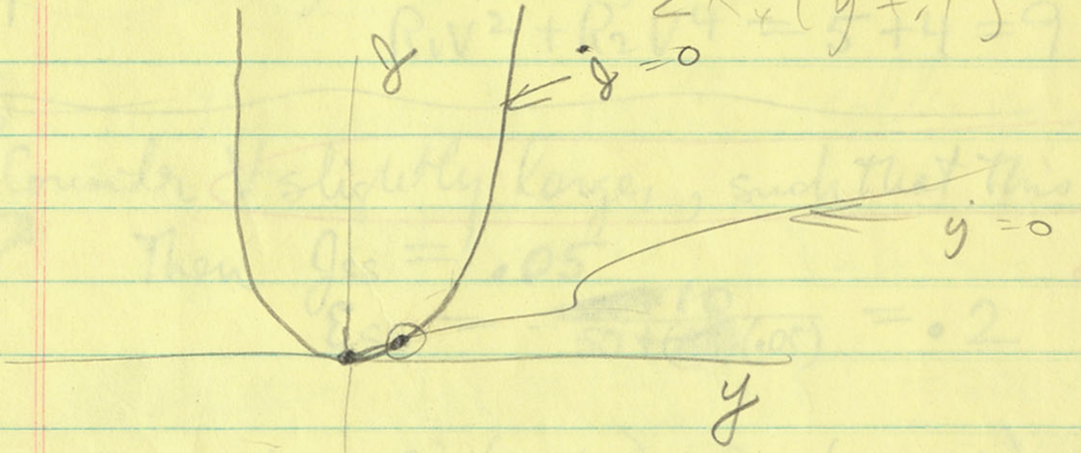
$$\dot{g} = 0, \quad k_5(k_1y^2+k_2y^4) = k_6g$$

$$\dot{y} = 0, \quad -y + \frac{k_1y^2+k_2y^4}{k_3+k_4g}(1-y) - g(y+.1) = 0$$

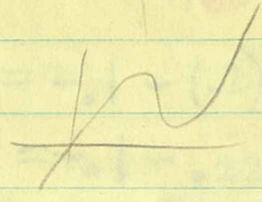
left this out

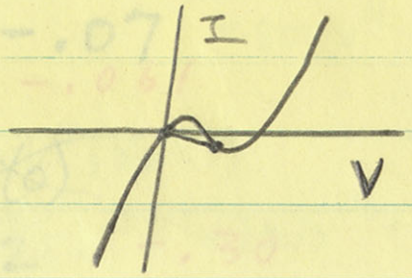
$$+k_4g^2(y+.1) + k_4yg + [k_3y - k_1y^2 - k_2y^4) = 0$$
$$+k_3(y+.1)g$$

$$g = \frac{-(k_3+k_4)y - .1k_3 \pm \sqrt{(\quad)^2 - 4k_4(y+.1)(\;)}}{2k_4(y+.1)}$$



?. $\dot{g}<0$, $g=0$: $\dot{g} = k_3k_5\varepsilon$





6/18/64

②

Take Series ⑤ or Series ⑦ and
examine for $V = 0.1$
$V = -0.1$

Series ⑤ $R_1 = 500.$
$R_2 = 4 \times 10^4$
$R_3 = 50$
$R_4 = 1.$
$R_5 = .05$ $\qquad R5/R6 = .005 = \frac{1}{200}$
$R_6 = 10.$

$$J_{ss} = \frac{R_5}{R_6}\left(R_1 V^2 + R_2 V^4\right) = .005\left(500V^2 + 4\times10^4 \cdot V^4\right)$$

$$\mathcal{E}_{ss} = \cancel{R_6/R_5}\ \frac{R_1 V^2 + R_2 V^4}{R_3 + R_4 J_{ss}} = \frac{(500v^2 + 4\times10^4 V^4)}{50 + J_{ss}}$$

for $V = \pm 0.1$, $V^2 = 10^{-2}$, $V^4 = 10^{-4}$
$R_1V^2 + R_2V^4 = 5 + 4 = 9$

Approx because { Consider V slightly larger, such that this $= 10$

Then $J_{ss} = .05$ $\qquad .045$

$$\mathcal{E}_{ss} = \frac{\cancel{.005}\ 10}{50 + \cancel{.05}(.05)} = .2 \qquad .18$$

$$\psi_{ss} = V_{ss} - \mathcal{E}_{ss}(1 - V_{ss}) + J_{ss}(V_{ss} + .1)$$

for $V_{ss} = .1$ $\qquad = .1 - (.2)(.9) + .05(.2)$
$= .1 - .18 + .01 = -.07$
$\quad .162 \quad .009 \quad -.061$

for $V_{ss} = -.1$ $\qquad \psi_{ss} = -.1 - (.2)(1.1) + \cancel{.05(0)}$
$= -.1 - \overset{.120}{.22} = -.32 \qquad -.30$

Consider $V = \pm 0.01$, $V^2 = 10^{-4}$, $V^4 = 10^{-8}$

$R_1 V^2 + R_2 V^4 = .05 + .0004 \approx .05$

Then $J_{ss} \cong 25 \times 10^{-5}$

$\mathcal{E}_{ss} = \frac{.05}{50} = 10^{-3}$

for $V = +.01$ $\quad \psi_{ss} = +.01 - 10^{-3}(.99) + 25 \times 10^{-5}(.11)$

$\simeq +.009$

for $V = -.01$ $\quad \psi_{ss} = -.01 - 10^{-3}(1.01) + 25 \times 10^{-5}(.09)$

$\simeq -.011$

$\therefore$ zero is approx where $\mathcal{E}_{ss} \simeq V_{ss} \approx \frac{500V^2 + 4 \times 10^4 V^4}{50}$

approx for $V \approx 10V^2$

Note: the three singular points really corresp. to cubic for $R_2 = 0$

consider first e.g. let $R_1 = 0$, then

for st st.

~~$\psi = V$~~ $\quad J_{ss} = \boxed{\frac{R_5}{R_6} R_2} V^4 = 200V^4$

$\mathcal{E}_{ss} = \frac{R_2 V^4}{R_3 + \frac{R_4}{R_2}\frac{R_5}{R_6} V^4} = \frac{4 \times 10^4 V^4}{50 + 200V^4}$

$\approx 8 \times 10^2 V^4$ for small V

$\approx 800V^4$

for small V st st. is $\psi = V - 800V^4(1-V) + 200V^4(V + .1)$

set $\psi = 0$, one root is $V = 0$ $\therefore$ leave ~~V^3~~ $10^3 V^4 - 780V^3 + 1 = 0$

for small V $V^4 - .78V^3 + 10^{-3} = 0$

Consider next $R_2 = 0$

Try $R_1 = 10^4$

Then $J_{ss} = 50V^2$

$$\mathcal{E}_{ss} = \frac{10^4 V^2}{50 + 50V^2} \approx 200V^2$$

for $V^2 << 1$

$$= \frac{200V^2}{1+V^2}$$

~~[illegible]~~ for st st.

~~$\psi = V - \frac{10^4 V^2}{50}$~~

$$\psi = V - \left(\frac{200V^2}{1+V^2}\right)(1-V) - 50V^2(V+.1)$$

for $\psi = 0$ get $0 = 1 - 200V\left(\frac{1-V}{1+V^2}\right) - 50V(V+.1)$

$$200V(1-V) = (1+V^2)(1 - 50V(V+.1))$$

$$-200V^2 + 200V = 1 + V^2 - 50V^2 - 5V - 50V^4 - 5V^3$$

But if $V^2 << 1$, get approx

$$-200V^2 + 200V = 1 - 50V^2 - 5V$$

$$-150V^2 + 205V - 1 = 0$$

approx $V^2 - 1.33V + .006 \simeq 0$

$$(V - 1.33)(V - .0045) \simeq 0$$

Comment:

May wish to run ~~[illegible]~~

One case with $R_1 = 10^4$, $R_2 = .1$

Another case with $R_1 = .1$, $R_2 = 4 \times 10^4$
$\times 10^{-4}$

But returning to pages ② & ③

There is a root between $V_{SS} = 0.1$
and $V_{SS} = 0.01$

Try $V_{SS} = .05$

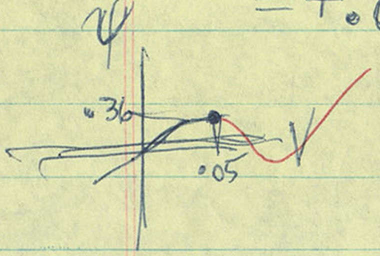
Then $V^2 = 25 \times 10^{-4}$ $V^4 = 625 \times 10^{-8}$

$R_1 V^2 = 1.25$ $R_4 V^4 \approx 10^{-5}$

$\therefore J_{SS} \approx \frac{1.25}{200} = .00625$

$\mathcal{E}_{SS} = \frac{1.25}{50 + \epsilon} = .025$

$\psi_{SS} = .05 - .025(.95) + .00625(.15)$
$= .059_4 - .023_7$
$= +.0357$



$\therefore$ middle root lies between ~~V=~~ $.05$
or $V = .1$

8/14/64

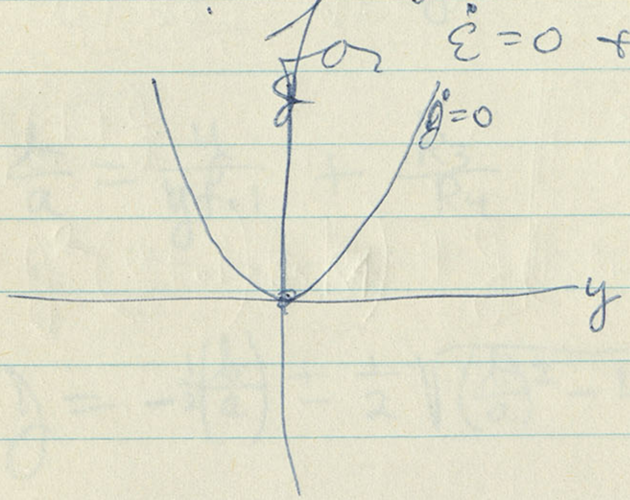
$\dot{\varepsilon}=0$ gives $\varepsilon = \frac{k_1y^2+k_2y^4}{k_3+k_4J}$

If $\dot{J}$ is also zero, then $\varepsilon = \frac{k_6J}{k_5(k_3+k_4J)}$

also, then $J = \frac{k_5}{k_6}(k_3+k_4J)\varepsilon = \frac{k_5}{k_6}(k_1y^2+k_2y^4)$

which gives a relation between J and y

for $\dot{\varepsilon}=0$ & $\dot{J}=0$



However, for $\dot{J} \neq 0$ but $\dot{y}=0$, & $\dot{\varepsilon}=0$ then get

$$0 = -y + (1-y)\left(\frac{k_1y^2+k_2y^4}{k_3+k_4J}\right) - J(y+.1)$$

$$0 = -k_3y - k_4yJ - \overset{k_3}{(yJ+.1J)} + (1-y)(k_1y^2+k_2y^4)$$

$$-k_4J^2(y+.1)$$

$\$$

$$k_4(y+.1)J^2 + (k_4y + k_3(y+.1))J + k_3y - (1-y)(k_1y^2+k_2y^4) = 0$$

$$J = \frac{-b \pm \sqrt{b^2 - 4ac}}{2a}$$

where $a = k_4(y + .1)$

~~b~~

$b = k_4 y + k_3(y + .1)$

$c = k_3 y - (1 - y)(k_1 y^2 + k_2 y^4)$

$$\frac{b}{a} = \frac{y}{y + .1} + \frac{k_3}{k_4}$$

$$J = -\frac{1}{2}\left(\frac{b}{a}\right) \pm \frac{1}{2}\sqrt{\left(\frac{b}{a}\right)^2 - 4\frac{c}{a}}$$

Notice that for $y = 0$, $c = 0$

$b = 0.1\,k_3$

$a = 0.1\,k_4$

and $J = \dfrac{-k_3 \pm k_3}{2k_4} = \begin{cases} 0 \\ \text{or } -\dfrac{k_3}{k_4} \end{cases}$

but we exclude $-J$ values for physical reasons extra 2a

throwing $\dot{j}=0$
similarly $\dot{y}=0$

for $\dot{j}=0$ $\quad \mathcal{E} = \dfrac{k_6 j}{k_5(k_3+k_4 j)}$

Better $\quad -y + \dfrac{k_6 j}{k_5(k_3+k_4 j)}(1-y) - j(y+.1) = 0$

~~$-y + k_6 j - k_6 j y$~~

$$(y + jy + .1j)(k_5)(k_3+k_4 j) = k_6 j(1-y)$$

~~$y(1+j$~~

$$j^2(y+.1)(k_5)(k_4) + j\left(k_5 k_4 y + k_5 k_3 (y+.1) \cancel{- k_6 y}\right.$$

$$\left. - k_6(1-y)\right) + k_3 k_5 y = 0$$

~~$j = -(k_4 k_5 y$~~

quadratic with

$a = k_4 k_5 (y+.1)$

$b = (k_6 + k_5(k_3+k_4))y + \dfrac{k_3 k_5}{10} - k_6$

$c = k_3 k_5 y$

$$j = \frac{-b \pm \sqrt{b^2 - 4ac}}{2a}$$

Before going away
≈ July 1, 1964

Hypothesis

Suppose there are not really two groups of branch lengths, *but* merely a wide range of variation.

Then the shortest lengths are least likely to be cut & are fairly likely to be shorter than the truncated lengths of the long cut branches. This might be the basis for group V

For those neurons with less variation in length (perhaps group III, also cases 3 & 4 of Monte Carlo neurons) the truncated lengths tend to be shorter than bifurcating lengths.

Plan cases 5, 6 & 7 to check this idea.

4/21/64

$\frac{2r}{h}$ suppose $h = 200$
suppose $r = 150$

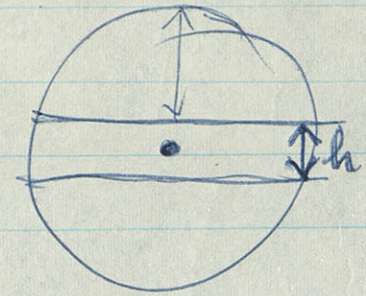
Then $\frac{2r}{h} = \frac{3}{2}$ i.e. $\frac{2}{3}$ not cut
$\frac{1}{3}$ cut

30 of 86 agrees pretty well with this.

If $r = 500$, so $\frac{2r}{h} = \frac{10}{2} = 5$
$\therefore$ chance of survival $= \frac{1}{5}$

$r = 800$, so $\frac{2r}{h} = \frac{16}{2} = 8$
chance of survival $= \frac{1}{8}$
provided tree is straight.

4/20/64



volume of sphere $= \frac{4}{3}\pi r^3$

volume of slab $\approx \pi r^2 h$

$\frac{3h}{4r} = \left(\frac{3}{4}\right)\left(\frac{h}{r}\right)$

ratio $\approx \frac{h}{\frac{4}{3}r} \approx \frac{2}{\frac{4}{3}\times 10} = \frac{3}{20} = .15$

hemisphere ~~vol~~ $= \frac{2}{3}\pi r^3$

let $z = r - \frac{h}{2}$ ~~let [illegible] h~~

spherical seg less centered slab = [illegible]

$\frac{1}{3}\pi z^2 (3r - z)$

Suppose $z = 0.9r$, get $\frac{1}{3}\pi (.81 r^2)(2.1 r)$

$= \frac{1}{3}\pi r^3 (1.7 \quad)$

$\therefore \frac{\text{seg}}{\text{hemisphere}} = \frac{1.7}{2}$

$\therefore \frac{\text{slab}}{\text{sphere}} = \frac{0.3}{2} = .15$

Except for V close to 1.

in particular, for V from .5 to .8

C max is occurs almost simultaneous with $\mathcal{E}$ max.

If make this simplifying assumption

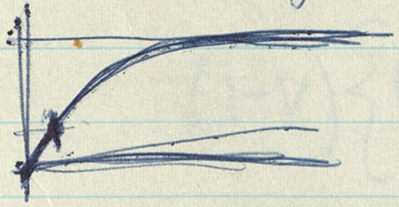
Then $\mathcal{E}(R_3 + R_4 J) = R_1 V^2 + R_2 V^4$

$$\tau \frac{dJ}{dt} = R_5 (R_1 V^2 + R_2 V^4) - R_6 J$$

~~and $\frac{dC}{dt} = 0 \simeq \frac{dJ}{dt}(V + .1)$~~

$$\tau \frac{dJ}{dt} = \text{const} - R_6 J$$

given an estimate of TK^*
can get an estimate of J.



Then $\tau \frac{d\mathcal{E}}{dt} = \text{const} - (R_3 + R_4 J)\mathcal{E}$.

get est. of $\mathcal{E}$
& plug into equation for C.

$$C = V - \varepsilon(1-V) + g(V+.1)$$

when $\frac{dc}{dt} = 0$

with clamped ~~then~~ voltage

$$\frac{dc}{dt} = 0 - \frac{d\varepsilon}{dt}(1-V) + \frac{dg}{dt}(V+.1)$$

$$\boxed{\frac{d\varepsilon}{dt}(1-V) = \frac{dg}{dt}(V+.1)}$$

$$\tau \frac{d\varepsilon}{dt} = (R_1 V^2 + R_2 V^4) - (R_3 + R_4 g)\varepsilon$$

$$\tau \frac{dg}{dt} = R_5 (R_3 + R_4 g)\varepsilon - R_6 g$$

$$(1-V)\left\{R_1 V^2 + R_2 V^4 - (R_3 + R_4 g)\varepsilon\right\} = (V+.1)\left\{R_5(R_3 + R_4 g)\varepsilon - R_6 g\right\}$$

9/10/64

mx 669
active

at soma $\left|\frac{+}{-}\right| = \left|\frac{1.13}{1.59}\right| = 0.71$

at glom. $\left|\frac{-}{+}\right| = \left|\frac{.285}{.385}\right| = 0.74$

peak to peak $\frac{\text{soma}}{\text{glom}} = \frac{2.72}{.67} = 4.06$

results from Shunt factor

666
passive

at soma $\left|\frac{+}{-}\right| = \left|\frac{.451}{1.43}\right| = 0.315$

at glom $\left|\frac{-}{+}\right| = \left|\frac{.115}{.345}\right| = 0.334$

peak to peak $\frac{\text{soma}}{\text{glom}} = \frac{1.88}{.46} = 4.09$

Peak Neg of data being used for figures

Depths			○	○
.3	18 mm		.400	.308
.41	23		.512	.393
.5	29.5		.656	.504
.56	33.5		.745	.570
.6	39.5		.880	.675
.64	45.	1.0		.770
.68	58.5	1		1.0
.74	59.			
.91	50.5			

if this were initial level

act.

64794.8827 Neg peak amplitudes Rel

Cp. No.	4	−.3415	1.000
	5	−.3329	.974
	6	−.2781	.813
	7	−.1979	.580 about half
	8	−.1136	.333
	9	−.0465	.136
	10	−.0279 flat	.082
	11	−.0424 reversed	.124
	12	−.0514	.150
	13	−.0568	.166
	14	−.0595	.174

$\frac{35}{10}$ 3.5

64791.0669 active

			+
Gpts	4	-1.5899	1.000
	5	-1.5726	.990
	6	-1.4606	.920
	7	-1.1778	.740
	8	-.5869	.370
	9	-.2846	.180

64791.0666 passive

			+
Opts	4	−1.4298	1.000
	5	−.7843	.550
	6	−.3729	.260
	7	−.1500	.105
	8	−.0968	.068
	9	−.1151	.080

Partial Differential Equations of Second Order

Laplace Equation (elliptic Type) (harmonic analytic)

$$u_{xx} + u_{yy} + u_{zz} = 0$$

Wave Equation (hyperbolic type)

$$u_{xx} + u_{yy} - u_{zz} = 0$$

Heat Equation (parabolic type)

$$u_z = u_{xx} + u_{yy}$$

Mixed Type $L(u) = a u_{xx} + 2b u_{xy} + C u_{yy}$

elliptic if $ac - b^2 > 0$

hyperbolic $ac - b^2 < 0$

parabolic $ac - b^2 = 0$

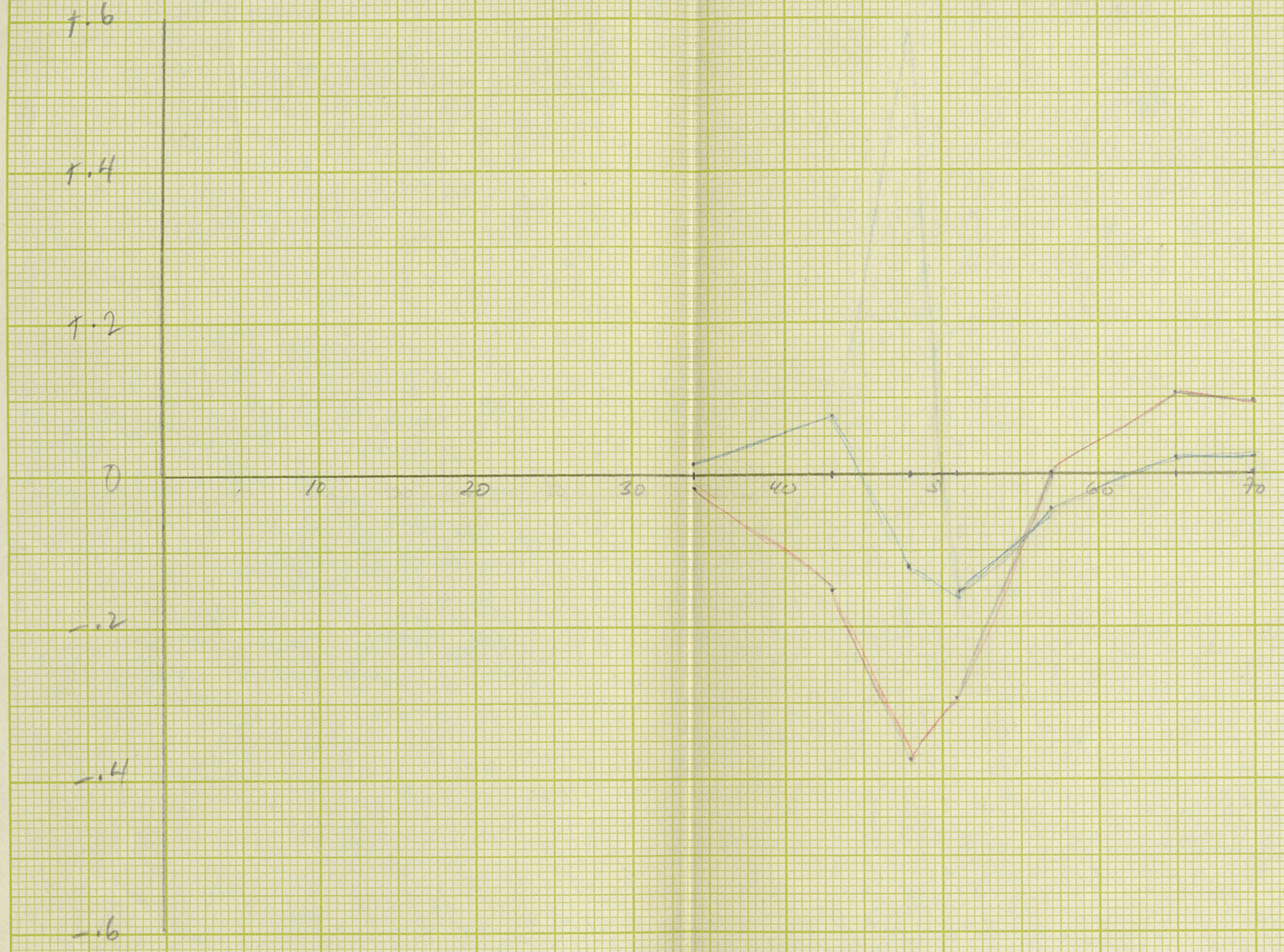
Calc. mod. of 64791.0666 passive

⑥

9/17/64

Blue is new pot. divider case (with prim. diluted by sec)

Red is old pot. divider case



64791.0666

9/17/64

At compartment 6

Begin with unshunted values

without potential divider

	KT 34	43	51	57	70	48	65
Value in 6 (A)	-.064	-.492	-.355	.109	.183	-.593	.212
7 (B)	-.026	-.209	-.210	.034	.094	-.306	.106
8 (C)	-.008	-.062	-.077	.006	.032	-.103	.035
4 (S)	-.256	-1.748	-.327	.503	.428	-1.141	.518
0.4 × A	-.026	-.196	-.142	.044	.073	-.237	.085
0.3 × B	-.008	-.063	-.063	.010	.028	-.092	.032
0.2 × C	-.002	-.012	-.015	.001	.006	-.021	.007
NU	-.036	-.271	-.220	.055	.107	-.350	.124

for potential divider shift.

P = 0.2 × S	-.051	-.349	-.065	.101	.085	-.228	.103
NU - P	+.015	.078	-.155	-.046	.022	-.122	.021

Compare with old shunted values (in ⑥)

-.016	-.151	-.294	.006	.096	-.373	.107